in Haller

Access DB# 83365

## **SEARCH REQUEST FORM**

## Scientific and Technical Information Center

Requester's Full Name: BEN Art Unit: 16 20 Phone Mail Box and Bldg/Room Location	SACKEY  Number 30 5 - 484  on: CMJ 3E 1/Re	Examiner #: 734867   129   29   Serial Number: 209   29   29   29   29   29   29   29	Date: <u>/2/3///2</u> ' <u>937 286</u> PAPER DISK E-MAIL
If m r than one search is sub			
Please provide a detailed statement of th Include the elected species or structures, utility of the invention. Define any term known. Please attach a copy of the cover	e search topic, and describ keywords, synonyms, acr s that may have a special	ne as specifically as possible the subjection onyms, and registry numbers, and cor meaning. Give examples or relevant of	ct matter to be searched. mbine with the concept or
Title of Invention: Cyclic &	elyceno phosp	hates and anal	1078 thereof
Inventors (please provide full names):	Mair S	hinit 2/4	
Earliest Priority Filing Date: 3	125/95		41-34
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+ ( 0 0 0 0 0 0 0 0 0 0 0 0 0	·; -c(= 0)- o+-, c+20 =	mis 0-3  Cyl, - CH2 cyl)  multy substituted as	
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STAFF USE ONLY Searcher:	Type of Search  NA Sequence (#)	Vendors and cost where	e applicable

No

2/6/03 Ben Sackey 1626 305 6889

28 Ben

L18 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS

431006

AN 1973:418684 CAPLUS DN 79:18684

TI Preparation and chemistry of 2,6,7-trioxa-1-phosphabicyclo[2.2.1]heptane

AU Denney, Donald B.; Varga, Sandor L.

CS Sch. Chem., Rutgers State Univ., New Brunswick, NJ, USA

SO Phosphorus and the Related Group V Elements (1973), 2(5-6), 245-8 CODEN: PHUSBV; ISSN: 0369-9722

DT Journal

LA English

GI For diagram(s), see printed CA Issue.

AB HOCH2CH, (OH) CH2OH was heated with (MeO) 3P in SF-96 silicone fluid at 115-120.degree. and the resulting 2,6,7-trioxa-1-phosphabicyclo[2.2.1] heptane oxidized with N2O4 to give the trioxaphosphabicycloheptane oxide I. I and MeOH gave the phosphate II.

RN 41852-35-1 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-methoxy-, 2-oxide (9CI) (CA.INDEX NAME)

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Ben

L18 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 2001:834204 CAPLUS

DN 136:145102

TI Neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells

AU Haimovitz, Rachel; Shinitzky, Meir

CS Department of Biological Chemistry, The Weizmann Institute of Science, Rehovot, 76100, Israel

SO Life Sciences (2001), 69(23), 2711-2723 CODEN: LIFSAK; ISSN: 0024-3205

PB Elsevier Science Inc.

DT Journal

LA English

AB A series of cyclic glycerophosphates and their deoxy analogs were tested for induction of neuronal outgrowth in PC12 cells. Under chronic presence

of a cyclic phosphate PC12 cells developed distinct isles of neuronal networks which covered up to 20% of the culture area, while .alpha. and .beta. glycerophosphates (the neg. control compds.) did not induce any neuronal outgrowth. Distinct isles of neuronal networks were also obsd. upon short term application (i.e. 2 pulses of 3 h each at day 1 and day

of the tested cyclic phosphates in contrast to an analogous short term exposure to NGF which was abortive. Anal. of tyrosine phosphorylation indicated a battery of phosphorylated proteins after several minutes of application of the cyclic phosphates, among which was an ERK protein of .apprx.63kD (possibly ERK7). Nerve rescue expts. were carried out with NGF differentiated PC12 cells where NGF was replaced with either 1,2 or 1,3 cyclic propanediolphosphate (1,2 cPP and 1,3 cPP) for 7 days. A distinct dose dependent preservation of neuronal network by these compds. was obsd. In the control cultures NGF deprivation resulted in massive neuronal retraction and cell death. Preliminary expts. indicated that

the

nerve rescue by the cyclic phosphates involves the increase in the level of CASPase 6. The above findings suggest that cyclic glycerophosphates and their analogs may bear important physiol. and pharmacol. implications which are currently under investigation.

IT 42320-97-8 286020-33-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells)

RN 42320-97-8 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 286020-33-5 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

```
ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN
     2000:706969 CAPLUS
DN
     133:261536
     Pharmaceutical compositions comprising cyclic glycerophosphates and
ΤI
     analogs thereof for promoting neural cell differentiation
IN
     Shinitzky, Meir
PA
     Yeda Research and Development Co. Ltd., Israel
SO
     PCT Int. Appl., 42 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
                                            APPLICATION NO. DATE
     PATENT NO.
                     KIND DATE
     _____
                                             _____
     WO 2000057865 A2 20001005
                                            WO 2000-IL185
                                                               20000324
PΙ
     WO 2000057865
                      A3 20010628
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
         W:
             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     BR 2000009296
                             20011218 BR 2000-9296
                                                               20000324
                       А
                                            EP 2000-912877
                                                                20000324
     EP 1162959
                        A2
                             20011219
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
                     T2
                             20021126
                                             JP 2000-607616
                                                               20000324
     JP 2002540146
PRAI IL 1999-129178
                       Α
                             19990325
     WO 2000-IL185
                             20000324
                        W
     MARPAT 133:261536
OS
     Cyclic glycerophosphates and analogs thereof (CGs) are shown to exert
     neural promoting activities in target cells. Such activities include
     promotion of neuronal outgrowth, promotion of nerve growth, provision of
     dopaminotrophic supporting environment in a diseased portion of the
brain,
     prevention of nerve degeneration and nerve rescue. These activities of
     the CGs render them useful for treatment of various disorders including
     but not limited to mental disorders such as, for example, schizophrenia,
     dementia or disorders resulting in learning disabilities. In addn.,
these
     CGs may be used for the treatment of neurodegenerative conditions such as
     Alzheimer's disease, Parkinson's disease, conditions resulting from
     exposure to harmful environmental factors or resulting from a mech.
     injury. The CGs may also be used to treat an individual suffering from a
     primary neurodegenerative condition in order to prevent or reduce the
     appearance of secondary degeneration in addnl. nerves ("nerve rescue").
     For example, neural outgrowth of PC12 cells was seen when cells were
grown
     in the presence of nerve growth factor (50 ng/mL) or 1,3-cyclic
     glycerophosphate (1 .mu.M), but not in the presence of linear
     .alpha.-glycerophosphate.
IΤ
     298701-05-0P
     RL: BAC (Biological activity or effector, except adverse); BPN
     (Biosynthetic preparation); BSU (Biological study, unclassified); SPN
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Ben

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

Ben

(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); USES (Uses)
 (compns. comprising cyclic glycerophosphates for promoting neural
 differentiation for therapeutic uses)
RN 298701-05-0 CAPLUS
CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide, barium salt (9CI) (CA
 INDEX NAME)

●x Ba

## IT 286020-33-5P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

(compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

RN 286020-33-5 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

NEWS 36

NEWS 37

NEWS 38

Dec 17

Dec 17

Dec 30 ISMEC no longer available

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TOXCENTER enhanced with additional content

Adis Clinical Trials Insight now available on STN

NEWS 39 Jan 13 Indexing added to some pre-1967 records in CA/CAPLUS NEWS 40 Jan 21 NUTRACEUT offering one free connect hour in February 2003 NEWS 41 Jan 21 PHARMAML offering one free connect hour in February 2003 NEWS 42 Jan 29 Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC NEWS 43 Feb 13 CANCERLIT is no longer being updated NEWS 44 Feb 24 METADEX enhancements NEWS 45 Feb 24 PCTGEN now available on STN NEWS 46 Feb 24 TEMA now available on STN NEWS 47 Feb 26 NTIS now allows simultaneous left and right truncation NEWS 48 Feb 26 PCTFULL now contains images NEWS 49 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results January 6 CURRENT WINDOWS VERSION IS V6.01a, NEWS EXPRESS CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002 NEWS HOURS STN Operating Hours Plus Help Desk Availability NEWS INTER General Internet Information NEWS LOGIN Welcome Banner and News Items NEWS PHONE Direct Dial and Telecommunication Network Access to STN NEWS WWW CAS World Wide Web Site (general information)

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FILE COVERS 1907 - 13 Mar 2003 VOL 138 ISS 11
FILE LAST UPDATED: 12 Mar 2003 (20030312/ED)
  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
=> s 1,3-cyclic glycerophosphate
       7465882 1
       5712254 3
       258238 CYCLIC
          8095 GLYCEROPHOSPHATE
L1
            2 1,3-CYCLIC GLYCEROPHOSPHATE
                 (1(W)3(W)CYCLIC(W)GLYCEROPHOSPHATE)
=> d ll 1-2 all
    ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS
     2000:706969 CAPLUS
DN
     133:261536
TТ
     Pharmaceutical compositions comprising cyclic glycerophosphates and
     analogs thereof for promoting neural cell differentiation
IN
     Shinitzky, Meir
PA
     Yeda Research and Development Co. Ltd., Israel
SO
     PCT Int. Appl., 42 pp.
     CODEN: PIXXD2
DT
    Patent
    English
LΑ
    ICM A61K031-00
IC
     1-11 (Pharmacology)
     Section cross-reference(s): 29, 63
FAN.CNT 1
     PATENT NO.
                  KIND DATE
                                          APPLICATION NO. DATE
    WO 2000057865 A2 20001005
WO 2000057865 A3 20010628
ΡI
                                          WO 2000-IL185 20000324
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            LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
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     EP 1162959
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            IE, SI, LT, LV, FI, RO
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                                          JP 2000-607616
                                                           20000324
PRAI IL 1999-129178
                    A 19990325
    WO 2000-IL185 W
                           20000324
    MARPAT 133:261536
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uses)

IT

Cell differentiation

Cyclic glycerophosphates and analogs thereof (CGs) are shown to exert AΒ neural promoting activities in target cells. Such activities include promotion of neuronal outgrowth, promotion of nerve growth, provision of dopaminotrophic supporting environment in a diseased portion of the prevention of nerve degeneration and nerve rescue. These activities of the CGs render them useful for treatment of various disorders including but not limited to mental disorders such as, for example, schizophrenia, dementia or disorders resulting in learning disabilities. In addn., these CGs may be used for the treatment of neurodegenerative conditions such as Alzheimer's disease, Parkinson's disease, conditions resulting from exposure to harmful environmental factors or resulting from a mech. injury. The CGs may also be used to treat an individual suffering from a primary neurodegenerative condition in order to prevent or reduce the appearance of secondary degeneration in addnl. nerves ("nerve rescue"). For example, neural outgrowth of PC12 cells was seen when cells were in the presence of nerve growth factor (50 ng/mL) or 1,3 -cyclic glycerophosphate (1 .mu.M), but not in the presence of linear .alpha.-glycerophosphate. cyclic glycerophosphate neuronal differentiation mental disorder; ST antipsychotic schizophrenia cyclic glycerophosphate; Alzheimer disease parkinsonism cyclic glycerophosphate Anti-Alzheimer's agents IT Antiparkinsonian agents Antipsychotics Mental disorder Nervous system agents Schizophrenia (compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses) Monoamines TT Neurotrophic factors RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses) ΙT Nerve (degeneration, prevention of; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses) Mental disorder IT (dementia; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses) IT Nerve (differentiation; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses) IT (disorder; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses) ΙT (dopaminergic, degeneration of; compns. comprising cyclic

glycerophosphates for promoting neural differentiation for therapeutic

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(inducers; compns. comprising cyclic glycerophosphates for promoting
        neural differentiation for therapeutic uses)
    Nerve, disease
IT
        (injury, neuronal rescue after; compns. comprising cyclic
        glycerophosphates for promoting neural differentiation for therapeutic
        uses)
     Cell differentiation
TT
     Cell differentiation
        (neuronal; compns. comprising cyclic glycerophosphates for promoting
        neural differentiation for therapeutic uses)
     Drug delivery systems
ΙT
        (oral; compns. comprising cyclic glycerophosphates for promoting
neural
        differentiation for therapeutic uses)
     Drug delivery systems
IT
        (osmotic pumps; compns. comprising cyclic glycerophosphates for
        promoting neural differentiation for therapeutic uses)
IT
     Cell proliferation
        (promotion of; compns. comprising cyclic glycerophosphates for
        promoting neural differentiation for therapeutic uses)
     Drug delivery systems
IT
        (topical; compns. comprising cyclic glycerophosphates for promoting
        neural differentiation for therapeutic uses)
IT
     298701-05-0P
     RL: BAC (Biological activity or effector, except adverse); BPN
     (Biosynthetic preparation); BSU (Biological study, unclassified); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
     PREP (Preparation); USES (Uses)
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        differentiation for therapeutic uses)
                                             118897-32-8P 123406-35-9P
     711-07-9P
                13507-10-3P
                               22227-09-4P
TΤ
                                                 298701-09-4P
                                                                 298701-78-7P
                                  298701-08-3P
     286020-33-5P
                    298701-06-1P
     RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
                                             59-92-7, biological studies
     51-61-6, Dopamine, biological studies
IT
     102-32-9, DOPAC 306-08-1, Homovanillic acid
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
     9001-86-9, Phospholipase C
ΙT
     RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
     (Uses)
         (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
     57-55-6, 1,2-Propanediol, reactions 96-26-4, Dihydroxyacetone
IΤ
     504-63-2, 1,3-Propanediol 770-12-7, Phenyl phosphorodichloridate
     819-83-0, Disodium .beta.-glycerophosphate 4799-67-1 14690-00-7,
     2-Benzyloxy-1,3-propanediol 22002-87-5
                                                26776-70-5, Dihydroxyacetone
     dimer
     RL: RCT (Reactant); RACT (Reactant or reagent)
         (compns. comprising cyclic glycerophosphates for promoting neural
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differentiation for therapeutic uses)
IT
     187976-16-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
    ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
L1
    1993:534139 CAPLUS
AN
     119:134139
DN
     Formation of 1,3-cyclic
TΙ
     glycerophosphate by the action of phospholipase C on
     phosphatidylglycerol
     Shinitzky, Meir; Friedman, Peter; Haimovitz, Rachel
ΑU
     Dep. Membrane Res. Biophys., Weizmann Inst. Sci, Rehovot, 76100, Israel
CS
     Journal of Biological Chemistry (1993), 268(19), 14109-15
SO
     CODEN: JBCHA3; ISSN: 0021-9258
DT
     Journal
     English
LА
     7-3 (Enzymes)
CC
     The action of phospholipase C (PLC) from Bacillus cereus on
AΒ
     phosphatidylglycerol (PG), derived from egg yolk phosphatidylcholine
(PC),
     was examd. in an ether-water mixt. The PLC cleavage of PG and PC
followed
     a Michaelis-Menten kinetics with apparent Vmax values per 1 .mu.g enzyme
     of 0.26 and 0.91 .mu.mol.min-1 and Km values of 10 and 12 mM, resp. When
     the same enzymic reaction was carried out in minimally buffered aq. soln.
     of 1% Triton X-100, the decrease in pH with respect to phospholipid
     cleavage was as expected with PC but much less pronounced with PG.
     could be accounted for by .alpha.-glycerophosphate, in the PLC hydrolysis
     of PG. Examn. of the chem. nature of the water-sol. product of PG by 31P
     NMR revealed a single band at 2.31 ppm, while the bands of
     .alpha.-glycerophosphate and .beta.-glycerophosphate appeared at 5.12 and
     4.57 ppm, resp. Basic hydrolysis of the phospholipase cleavage product
of
     PG (0.1 M NaOH for 1 min at 80 .degree.C) followed by neutralization
     shifted its 31P NMR band to 5.18 ppm, which practically coincided with
     that of .alpha.-glycerophosphate. Analogous expts. were carried out with
     PG labeled with 3H at the carbon 2 of the glycerol headgroup ([3H]PG).
     Autoradiog. of thin layer chromatog. (TLC) of the [3H]PG enzymic
     hydrolyzate displayed a single 3H-labeled compd., which could be
converted
     to .alpha.-glycerophosphate by basic hydrolysis. These results strongly
     suggest that the phosphate headgroup of PG is cleaved off by PLC as
     1,3-cyclic glycerophosphate. A
     series of PLC expts. with phosphatidyldihydroxyacetone and phosphatidyl
     1,3-propanediol as model substrates supported this assignment.
     Two-dimensional homonuclear 1H NMR correlated spectra as well as IR
     spectra carried out on the isolated sodium salt of this product could
     further confirm such a structure. The unique structure and chem. nature
     of 1,3-cyclic glycerophosphate may
     bear a distinct physiol. function.
     cyclic glycerophosphate formation phospholipase C phosphatidylglycerol
st
     Phosphatidylglycerols
IT
     RL: RCT (Reactant); RACT (Reactant or reagent)
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Page 7

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(cleavage of, by phospholipase C, cyclic glycerophosphate formation
in)
IT
    Michaelis constant
        (of phospholipase C, with phosphatidylglycerol)
     Phosphatidylcholines, reactions
IT
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with phospholipase C, kinetics of, phosphatidylglycerol
        in relation to)
     9001-86-9, Phospholipase C
IT
     RL: BIOL (Biological study)
        (cyclic glycerophosphate formation by, of Bacillus cereus, in
        phosphatidylglycerol cleavage)
ΙT
     42320-97-8
     RL: FORM (Formation, nonpreparative)
        (formation of, by phospholipase C cleavage of phosphatidylglycerol)
IT
     149864-37-9
     RL: FORM (Formation, nonpreparative)
        (formation of, by phospholipase C cleavage of
        phosphatidylhydroxyacetone)
     13507-10-3
ΙT
     RL: FORM (Formation, nonpreparative)
        (formation of, by phospholipase C cleavage of phosphatidylpropanediol)
=>
---Logging off of STN---
Executing the logoff script...
=> LOG Y
                                                  SINCE FILE
                                                                  TOTAL
COST IN U.S. DOLLARS
                                                                 SESSION
                                                       ENTRY
                                                                  13.79
                                                       13.58
FULL ESTIMATED COST
                                                  SINCE FILE
                                                                   TOTAL
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
                                                       ENTRY
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                                                                   -1.30
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STRUCTURE FILE UPDATES: 20 JAN 2003 HIGHEST RN 479577-81-6 DICTIONARY FILE UPDATES: 20 JAN 2003 HIGHEST RN 479577-81-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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FILE COVERS 1907 - 21 Jan 2003 VOL 138 ISS 4 FILE LAST UPDATED: 20 Jan 2003 (20030120/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que 124

STR

2 1 C G1 CH2 08 07

2, 167 structures from this query

REP G1=(0-3) C NODE ATTRIBUTES: CONNECT IS E1 RC AT 8 DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

CH2-OH @10 11

NUMBER OF NODES IS 8

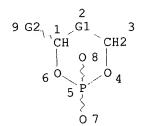
STEREO ATTRIBUTES: NONE

L5 2167 SEA FILE=REGISTRY SSS FUL L3

L16

STR

CH2·C~~O @16 17 18 5 utset search 2/39 structures



CH2·O~~C~~O @12 13 14 15

REP G1=(0-3) C
VAR G2=H/AK/10/12/16
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 8
CONNECT IS E1 RC AT 15
CONNECT IS E1 RC AT 18
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

L18 2139 SEA FILE=REGISTRY SUB=L5 SSS FUL L16

L19 1246 SEA FILE=HCAPLUS ABB=ON L18

L20 30 SEA FILE=HCAPLUS ABB=ON L19(L)THU/RL

L21 715 SEA FILE=HCAPLUS ABB=ON L19(L) (PREP OR SPN OR IMF)/RL

L24 21 SEA FILE=HCAPLUS ABB=ON L20 AND L21

=> d 124 all 1-21 hitstr

prep for therapeuticuse

L24 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2003 ACS AN 2002:955399 HCAPLUS

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

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Sackey 09/937386 Page 3
```

```
DN
    Hyaluronic acid production enhancer as skin protectant
ΤI
    Tanaka, Shinji; Murobuse, Kimiko; Kobayashi, Akiyuki
IN
     NOF Corporation, Japan
PA
     Jpn. Kokai Tokkyo Koho, 20 pp.
     CODEN: JKXXAF
DT
     Patent
     Japanese
LA
     ICM A61K031-661
IC
     ICS A61K038-00; A61P017-02; A61P043-00; C07F009-6574
     1-12 (Pharmacology)
CC
     Section cross-reference(s): 24
FAN.CNT 1
                                          APPLICATION NO. DATE
     PATENT NO.
                     KIND DATE
                                           _____
                      ____
                                           JP 2001-171689
                                                            20010606
     JP 2002363081
                     A2
                            20021218
                          20010606
PRAI JP 2001-171689
CH<sub>2</sub>OR
CH2O P.
       O I
     Skin protectants in the treatment of atrophy of the skin induced by aging
     or steroid and in the prevention of the scar formation after the healing
     of wound which contain as the active ingredient cyclic phosphatide derivs.
     represented by the following general formula I (RO = C8-22 alc. residue or
     fatty acid residue; M = H, alkali metal, alk. earths metal, and
     (substituted) ammonium) as hyaluronic acid prodn. enhancer, hyaluronic
     acid synthetase gene promoter, and cellular activator are offered.
     cyclic phosphatide deriv hyaluronate enhancer skin protectant
ST
     Skin, disease
ΙT
        (aging; cyclic phosphatide as hyaluronic acid prodn. enhancer for
        protecting skin)
     Skin, disease
IT
        (atrophy; cyclic phosphatide as hyaluronic acid prodn. enhancer for
        protecting skin)
     Cell activation
ΙT
     Wound healing promoters
        (cyclic phosphatide as hyaluronic acid prodn. enhancer for protecting
        skin)
     Phosphatidic acids
IT
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
         (cyclic, derivs.; cyclic phosphatide as hyaluronic acid prodn. enhancer
        for protecting skin)
     Gene, animal
 ΙT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
         (hyaluronic acid synthetase; cyclic phosphatide as hyaluronic acid
```

(scar; cyclic phosphatide as hyaluronic acid prodn. enhancer for

(synergistic; cyclic phosphatide as hyaluronic acid prodn. enhancer for

Skin, disease

protecting skin)

Drug interactions

IT

ΙT

prodn. enhancer for protecting skin)

protecting skin) 9004-61-9, Hyaluronic acid 39346-43-5, Hyaluronic acid synthetase ΙT RL: BSU (Biological study, unclassified); BIOL (Biological study) (cyclic phosphatide as hyaluronic acid prodn. enhancer for protecting skin) 106096-93-9P, Basic fibroblast growth factor 168217-08-1P IT 168217-09-2P 169736-88-3P 478336-74-2P 478336-75-3P 478336-76-4P 478336-77-5P 478336-78-6P 478336-79-7P 478336-80-0P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (cyclic phosphatide as hyaluronic acid prodn. enhancer for protecting skin) 506-03-6, 1-0-sn-Hexadecylglycerol ΙT RL: RCT (Reactant); RACT (Reactant or reagent) (cyclic phosphatide as hyaluronic acid prodn. enhancer for protecting skin) 168217-08-1P 168217-09-2P 169736-88-3P TΤ 478336-74-2P 478336-75-3P 478336-76-4P 478336-77-5P 478336-78-6P 478336-79-7P 478336-80-0P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (cyclic phosphatide as hyaluronic acid prodn. enhancer for protecting skin) RN 168217-08-1 HCAPLUS Hexadecanoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

RN 168217-09-2 HCAPLUS
9-Hexadecenoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (9Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

$$(CH_2)_{7}$$
  $(CH_2)_{5}$   $(CH_2)_{5}$ 

Na

RN 169736-88-3 HCAPLUS

CN 9-Octadecenoic acid (9Z)-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

HO P R O (CH<sub>2</sub>)
$$\frac{0}{7}$$
 Z (CH<sub>2</sub>) $\frac{7}{7}$  Me

Na

RN 478336-74-2 HCAPLUS

CN 5,8,11,14,17-Eicosapentaenoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

HO P R (CH<sub>2</sub>) 
$$\frac{z}{z}$$
  $\frac{z}{z}$ 

Na

PAGE 1-B

RN 478336-75-3 HCAPLUS

CN 4,7,10,13,16,19-Docosahexaenoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (4Z,7Z,10Z,13Z,16Z,19Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

Na

PAGE 1-B

RN 478336-76-4 HCAPLUS

CN 1,3,2-Dioxaphospholane, 4-[(hexadecyloxy)methyl]-2-hydroxy-, 2-oxide, sodium salt, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

RN 478336-77-5 HCAPLUS

CN

1,3,2-Dioxaphospholane, 4-[[(9Z)-9-hexadecenyloxy]methyl]-2-hydroxy-, 2-oxide, sodium salt, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

Na

RN 478336-78-6 HCAPLUS

CN 1,3,2-Dioxaphospholane, 2-hydroxy-4-[[(9Z)-9-octadecenyloxy]methyl]-, 2-oxide, sodium salt, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

Na

RN 478336-79-7 HCAPLUS

CN 1,3,2-Dioxaphospholane, 4-[[(5Z,8Z,11Z,14Z,17Z)-5,8,11,14,17-eicosapentaenyloxy]methyl]-2-hydroxy-, 2-oxide, sodium salt, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

Na

PAGE 1-B



RN 478336-80-0 HCAPLUS

CN 1,3,2-Dioxaphospholane, 4-[(4Z,7Z,10Z,13Z,16Z,19Z)-4,7,10,13,16,19-docosahexaenyloxy]methyl]-2-hydroxy-, 2-oxide, sodium salt, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

Na

PAGE 1-B



L24 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:693051 HCAPLUS

DN 135:242705

TI Phosphate based biodegradable polymers, their preparation and compositions with a biologically active substance

IN Leong, Kam; Jie, Wen; Zhuo, Ren-Xi; Mao, Hai-Quan

PA Johns Hopkins University, USA

SO PCT Int. Appl., 126 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K009-00

ICS A61K009-14; A61K009-16; A61M005-00; C08G079-04

CC 35-7 (Chemistry of Synthetic High Polymers)

Section cross-reference(s): 63

FAN.CNT 1

t MN.	PATENT NO.			KIND DATE					A!	PPLI	CATIO	o. 1	DATE						
													20010210						
PΙ				A2 20010920															
		W:	ΑE,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	ВĠ,	BR,	BY,	CA,	CH,	CN,	CO,	CU,	
			CZ,	DE,	DK,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	
			IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	
			MK,	MN,	MW,	MX,	NO,	ΝZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	
			ТJ,	TM,	TR,	TT,	UA,	UG,	UZ,	VN,	YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	
			MD,	RU,	TJ,	TM													
		RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	ΒE,	CH,	CY,	
			DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	
			ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	G₩,	ML,	MR,	ΝE,	SN,	TD,	TG			
	US 2002155092			A1 20021024				US 2001-803358 20010310											

```
Sackey 09/937386 Page 9
                            20000310
PRAI US 2000-188477P
    Biodegradable polymers comprise repeat units derived from cyclic phosphate
    monomers and, optionally, repeat units derived from lactide or
     caprolactone monomers. Articles and microspheres are prepd. from
     biodegradable polymers and polymer compns. Controlled release of a biol.
     active substance is achieved using the biodegradable polymers.
     D,L-lactide and ethylene Me phosphate (prepn. given) were polymd. in the
     presence of aluminum triisopropoxide under Ar at 140-160.degree..
     lactide ethylene methyl phosphate copolymer manuf property; ethylene
ST
     methyl phosphate prepn polymn; block polymn lactide ethylene methyl
     phosphate; ring opening polymn lactide ethylene methyl phosphate
ΙT
     Polymers, preparation
     RL: IMF (Industrial manufacture); PRP (Properties); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (biodegradable, biocompatible; phosphate-based biodegradable polymers
        for controlled-release of biol. active substances)
     Polymerization
ΙT
        (block; of lactide and ethylene Me phosphate)
     Drug delivery systems
TΤ
        (controlled-release; phosphate-based biodegradable polymers for)
     Glass transition temperature
IT
     Polymer degradation
        (of phosphate-based biodegradable polymers for controlled-release of
        biol. active substances)
IT
     Polyesters, preparation
     RL: IMF (Industrial manufacture); PRP (Properties); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (phosphate-based biodegradable polymers for controlled-release of biol.
        active substances)
ΙT
     Polymerization
        (ring-opening; of lactide and ethylene Me phosphate)
     361186-26-7P
TΤ
     RL: IMF (Industrial manufacture); PREP (Preparation)
        (phosphate-based biodegradable polymers for controlled-release of biol.
        active substances)
     220490-57-3P, Lactide-ethylene methyl phosphate copolymer
ΙT
     361186-24-5P 361186-25-6DP, demethylation
     RL: IMF (Industrial manufacture); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (phosphate-based biodegradable polymers for controlled-release of biol.
        active substances)
ΙT
     822-39-9P
                 6609-64-9P
     RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT
     (Reactant or reagent)
        (phosphate-based biodegradable polymers for controlled-release of biol.
        active substances)
     326604-67-5, Lactide-ethyl ethylene phosphate copolymer
ΙT
     RL: PRP (Properties)
        (phosphate-based biodegradable polymers for controlled-release of biol.
        active substances)
     100-01-6, p-Nitroaniline, biological studies
ΙT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (phosphate-based biodegradable polymers for controlled-release of biol.
        active substances)
ΙT
     361186-25-6P
     RL: IMF (Industrial manufacture); PRP (Properties); THU
      (Therapeutic use); BIOL (Biological study); PREP
```

(prepn. and block polymn.; phosphate-based biodegradable polymers for

(Preparation); USES (Uses)

controlled-release of biol. active substances) 2196-04-5P, Ethylene methyl phosphate IT RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent) (prepn. and polymn.; phosphate-based biodegradable polymers for controlled-release of biol. active substances) 7719-12-2, Phosphorus trichloride IT RL: RCT (Reactant); RACT (Reactant or reagent) (reaction with ethylene glycol; phosphate-based biodegradable polymers for controlled-release of biol. active substances) 107-21-1, Ethylene glycol, reactions IT RL: RCT (Reactant); RACT (Reactant or reagent) (reaction with phosphorus trichloride; phosphate-based biodegradable polymers for controlled-release of biol. active substances) ΙT 361186-26-7P RL: IMF (Industrial manufacture); PREP (Preparation) (phosphate-based biodegradable polymers for controlled-release of biol. active substances) 361186-26-7 HCAPLUS RN 2-Oxepanone, polymer with 2-ethoxy-1,3,2-dioxaphospholane 2-oxide, block CN (CA INDEX NAME) (9CI) CM1 CRN 823-31-4 CMF C4 H9 O4 P 2 CM CRN 502-44-3 CMF C6 H10 O2



CM 1

CRN 2196-04-5 CMF C3 H7 O4 P

CM 2

CRN 95-96-5 CMF C6 H8 O4

RN 361186-24-5 HCAPLUS

CN 1,3,2-Dioxaphospholane, 2-methoxy-, 2-oxide, polymer with .alpha.-hydro-.omega.-hydroxy[poly(oxy-1,2-ethanediyl)] disodium salt, block (9CI) (CA INDEX NAME)

CM 1

CRN 50856-01-4 CMF (C2 H4 O)n H2 O . 2 Na CCI PMS

$$HO = \begin{bmatrix} CH_2 - CH_2 - O \end{bmatrix}_n H$$

●2 Na

CM 2

CRN 2196-04-5 CMF C3 H7 O4 P

RN 361186-25-6 HCAPLUS

CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, (3S,6S)-, polymer with 2-methoxy-1,3,2-dioxaphospholane 2-oxide, block (9CI) (CA INDEX NAME)

CM 1

CRN 4511-42-6 CMF C6 H8 O4

Absolute stereochemistry.

CM 2

CRN 2196-04-5 CMF C3 H7 O4 P

IT 361186-25-6P

RL: IMF (Industrial manufacture); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and block polymn.; phosphate-based biodegradable polymers for controlled-release of biol. active substances)

RN 361186-25-6 HCAPLUS

CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, (3S,6S)-, polymer with 2-methoxy-1,3,2-dioxaphospholane 2-oxide, block (9CI) (CA INDEX NAME)

CM 1

CRN 4511-42-6 CMF C6 H8 O4

Absolute stereochemistry.

CM 2

CRN 2196-04-5 CMF C3 H7 O4 P

L24 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2003 ACS AN 2001:380438 HCAPLUS DN 135:24657 Selective cellular targeting: multifunctional delivery vehicles ΤI Glazier, Arnold PA Drug Innovation + Design, Inc., USA SO PCT Int. Appl., 981 pp. CODEN: PIXXD2 DΤ Patent LA English ICM A61K047-48 IC 63-5 (Pharmaceuticals) Section cross-reference(s): 1, 2, 8, 15, 25, 28 FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. -----WO 2000-US31262 20001114 A2 20010525 PΙ WO 2001036003 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

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SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                                            20001114
    AU 2001016075
                            20010530
                                           AU 2001-16075
                      Α5
                                           EP 2000-978631
                                                           20001114
                            20021113
    EP 1255567
                       A1
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                            19991115
PRAI US 1999-165485P
     US 2000-239478P
                            20001011
                      Ρ
     US 2000-241937P
                      Ρ
                            20001020
                       W
                            20001114
     WO 2000-US31262
     The present invention relates to the compns., methods, and applications of
AB
     a novel approach to selective cellular targeting. The purpose of this
     invention is to enable the selective delivery and/or selective activation
     of effector mols. to target cells for diagnostic or therapeutic purposes.
     The present invention relates to multi-functional prodrugs or targeting
     vehicles wherein each functionality is capable of enhancing targeting
     selectivity, affinity, intracellular transport, activation or
     detoxification. The present invention also relates to ultralow dose,
     multiple target, multiple drug chemotherapy and targeted immunotherapy for
     cancer treatment.
     antitumor drug targeting delivery vehicle
ST
     Multidrug resistance proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (MDR1, inhibitors; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
     Glycoproteins, specific or class
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (P170, inhibitors; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
     Prostate gland
TΤ
        (adenocarcinoma; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
IT
     Receptors
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (cell-surface; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
     Cholecystokinin receptors
ΙT
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
        (cholecystokinin B; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
     Proteins, specific or class
IT
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
         (complexes; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
     Proteins, specific or class
IT
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
         (fibroblast-activating; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
ΙT
     Receptors
```

```
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (folate; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
TΤ
     Receptors
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
        (for bombesin-releasing peptide; multifunctional delivery vehicles for
        selective cellular targeting of drugs)
TΤ
     Receptors
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (for gastrin-releasing peptide; multifunctional delivery vehicles for
        selective cellular targeting of drugs)
     Transport proteins
IT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (for nucleosides, inhibitors; multifunctional delivery vehicles for
        selective cellular targeting of drugs)
IT
     Biological transport
        (intracellular; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
TΤ
     Antibodies
     RL: BPR (Biological process); BSU (Biological study, unclassified); PEP
     (Physical, engineering or chemical process); THU (Therapeutic use); BIOL
     (Biological study); PROC (Process); USES (Uses)
        (monoclonal; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
     Antitumor agents
TΤ
     Cell division
     Chelating agents
     Cytotoxic agents
     Drug targeting
     Imaging agents
     Immunization
     Immunostimulants
         (multifunctional delivery vehicles for selective cellular targeting of
     Enzymes, biological studies
IT
     RL: BAC (Biological activity or effector, except adverse); BOC (Biological
     occurrence); BSU (Biological study, unclassified); BIOL (Biological
     study); OCCU (Occurrence)
         (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
     Laminin receptors
ΙT
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
      (Process)
         (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
ΙT
     MSH receptors
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
      (Process)
         (multifunctional delivery vehicles for selective cellular targeting of
         drugs)
      P-glycoproteins
TT
```

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Prostate-specific antigen

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Somatostatin receptors

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Biopolymers

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)

(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Anthracyclines

Radionuclides, biological studies

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Antigens

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(neoantigens; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Receptors

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(nitrobenzylthioinosine-binding; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Transport proteins

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(norepinephrine-transporting; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Benzodiazepine receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(peripheral; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Drug delivery systems

(prodrugs; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Proliferation inhibition

(proliferation inhibitors; multifunctional delivery vehicles for selective cellular targeting of drugs)

IT Ligands

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC

(Process)

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targeting of drugs)
     Drug delivery systems
IT
        (targeted; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
IT
     Nucleosides, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (transport proteins; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
IT
     Antigens
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
        (tumor-assocd.; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
ΙT
     Vaccines
        (tumor; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
     Biological transport
ΙT
        (uptake; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
     Antitumor agents
ΙT
        (vaccines; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
     Opioid receptors
ΙT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (.sigma.-opioid; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
IT
     Integrins
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
        (.alpha.v.beta.3; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
     9001-01-8, Kallikrein
ΙT
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (2, human glandular; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
     9024-62-8, Orotidine 5'-phosphate decarboxylase
                                                       9029-03-2, Dihydroorotic
ΙT
                          9032-02-4
     acid dehydrogenase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitors; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
ΙT
     342397-39-1P
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); PEP (Physical, engineering
     or chemical process); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
     23214-92-8DP, immucillin G derivs.
                                          209799-75-7DP, doxorubicin derivs.
IT
                                   341549-71-1P
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     341990-94-1P 341990-96-3P 341990-98-5P
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(targetable; multifunctional delivery vehicles for selective cellular

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    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
    study, unclassified); PNU (Preparation, unclassified); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
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                                                 342392-57-8P
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    341549-26-6P
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
    study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
    BIOL (Biological study); PREP (Preparation); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
    9001-12-1, collagenase
                             9001-77-8
                                         9001-92-7, proteinase
                                                                 9002-07-7,
ΙT
              9004-06-2, Elastase 9004-08-4, cathepsin
                                                          9025-26-7,
    trypsin
                  9025-62-1, Steroid sulfatase 9030-23-3, Thymidine
    cathepsin d
                                                      9039-53-6, urokinase
    phosphorylase
                    9031-61-2, Thymidylate synthase
     9040-48-6, Gelatinase 9045-77-6, Fatty acid synthase
                                                             9047-22-7,
                  9074-87-7, glutamate carboxypeptidase II
                                                             60616-82-2,
    cathepsin b
                                   79955-99-0, Stromelysin 1
                                                                84419-03-4,
    cathepsin L
                   62229-50-9, Egf
                          94716-09-3, cathepsin k 115926-52-8,
     quanidinobenzoatase
     Phosphatidylinositol 3-kinase 141256-52-2, matrilysin
                                                              141907-41-7,
    matrix metalloproteinase 142008-29-5, Protein kinase a 142243-02-5,
                 142805-58-1, Map kinase kinase 145267-01-2, stromelysin 3
    Map kinase
     146480-35-5, Gelatinase A 162032-86-2, cathepsin O 175449-82-8,
                    241475-96-7, Matriptase
     Collagenase 3
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
     9001-90-5, plasmin
IT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (multifunctional delivery vehicles for selective cellular targeting of
                           57-22-7, Vincristine 58-85-5D, Biotin, masked
ΙT
     50-07-7, Mitomycin c
                                                     518-28-5D,
               59-30-3D, Folic acid, masked derivs.
                                519-23-3D, Ellipticine, derivs.
     Podophyllotoxin, derivs.
                   7689-03-4, Camptothecin 10159-53-2D, Phosphoramide
                      11116-31-7D, Bleomycin A2, derivs. 24280-93-1,
     mustard, analogs
     Mycophenolic acid
                        33069-62-4D, Taxol, derivs.
                                                     52128-35-5, Trimetrexate
     65271-80-9D, Mitoxantrone, derivs. 77327-05-0, Didemnin B
                                                                  112953-11-4
     114899-77-3D, Ecteinascidin 743, derivs. 124689-65-2D, analogs
     139987-54-5, BW 1843U89
                              175795-76-3
                                           236743-94-5, Phthalascidin
     265646-19-3, Indanocine
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
     use); BIOL (Biological study); PROC (Process); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
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ΙT
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RL: PNU (Preparation, unclassified); RCT (Reactant); THU (Therapeutic
use); BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
    (multifunctional delivery vehicles for selective cellular targeting of
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        (multifunctional delivery vehicles for selective cellular targeting of
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     341549-57-3P
                    341549-58-4P
                    341549-63-1P
                                   341549-74-4P
                                                   341549-76-6P
                                                                  341549-78-8P
     341549-62-0P
                                                                  341549-83-5P
     341549-79-9P
                    341549-80-2P
                                   341549-81-3P
                                                   341549-82-4P
                    341549-85-7P
     341549-84-6P
                                   341549-86-8P
     RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
                                                    110914-51-7
                                       3588-30-5
                                                                  121031-01-4
                           3326-32-7
ΙT
     51-67-2
               2495-35-4
                                341549-30-2
                                                341549-33-5
                                                              341549-39-1
                   341549-28-8
     178623-11-5
     341549-73-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
                                 341549-29-9P
                                                 341549-31-3P
                                                                341549-32-4P
                  173039-08-2P
     5621-44-3P
ΙT
                    341549-36-8P
                                   341549-37-9P
                                                   341549-38-0P
                                                                  341549-40-4P
     341549-34-6P
     341549-69-7P
                    341549-70-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
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IT
    341549-72-2P
    RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        druas)
                                               341549-44-8
                                 341549-43-7
                                                             341549-45-9
                   341549-42-6
ΙT
     341549-41-5
                                 341549-48-2
                                               341549-49-3
                                                              341549-50-6
                   341549-47-1
     341549-46-0
                                 341549-65-3
                                               341549-66-4
                                                             341549-67-5
                   341549-64-2
     341549-51-7
                   341549-77-7
                                 341990-71-4
                                               342392-74-9
                                                             342393-39-9
     341549-68-6
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
     9001-78-9, Alkaline phosphatase
IT
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (placental type; multifunctional delivery vehicles for selective
        cellular targeting of drugs)
ΙT
     38048-32-7
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (receptors; multifunctional delivery vehicles for selective cellular
        targeting of drugs)
     341549-52-8P 341552-87-2P 341553-15-9P
IT
     341553-47-7P 341553-59-1P 341990-94-1P
     341990-96-3P 341990-98-5P 341990-99-6P
     341991-00-2P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PNU (Preparation, unclassified); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
RN
     341549-52-8 HCAPLUS
     Butanedioic acid, [[5-[[[[4-[(3S,19S)-19-amino-38-[2-[[(2R)-2-
CN
     (acetylamino)-3-(dimethylamino)-3-oxopropyl]dithio]-5-[[[[[(2E)-2,3-
     dihydro-2-[(4-hydroxy-3,5-dimethylphenyl)methylene]-5,6-dimethoxy-1-oxo-1H-
     inden-7-yl]amino]carbonyl]oxy]methyl]phenyl]-3-[(9H-fluoren-9-
     ylmethoxy) carbonyl]-1,6,17,20,34-pentaoxo-10,13,24,27,30,36-hexaoxa-
     2,7,16,21,33-pentaazaoctatriacont-1-yl]phenyl][(2-amino-1,4-dihydro-4-oxo-
     6-pteridinyl)methyl]amino]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-
     dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester
     (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.
Double bond geometry as shown.

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RN 341552-87-2 HCAPLUS
9,12,22,25,28,31,41-Heptaoxa-2,6,15,19,34,38,44-heptaaza-48phosphadopentacontane-3,50,52-tricarboxylic acid, 1-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[[(3-carboxy-1-oxopropoxy)methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]phenyl]-18-[18-[7-[[[[[2-(1,3-dicarboxypropyl)-2,3-dihydro-1-oxo-1H-isoindol-5-yl][(1,2-dihydro-3-methyl-1-oxobenzo[f]quinazolin-9-yl)methyl]amino]carbonyl]oxy]methyl]-5,8-dihydro-5,8-dioxo-2-naphthalenyl]-1,14-dioxo-5,8,11-trioxa-2,15-diazaoctadec-1-yl]-35-(1,14-dioxo-5,8,11-trioxa-2,15-diazadocos-1-yl)-48-hydroxy-1,5,16,20,33,37,45-heptaoxo-, 48-oxide, (3S,18S,35S)- (9CI) (CA INDEX NAME)

NH<sub>2</sub>

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Me

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CN

RN 341553-15-9 HCAPLUS

11,14,24,27,30,33,43,46,49-Nonaoxa-2,7,17,21,36,40,52-heptaaza-56-phosphahexacontane-3,58,60-tricarboxylic acid, 1-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[[(3-carboxy-1-oxopropoxy)methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]phenyl]-20-[17-[6-[[[[2-(1,3-dicarboxypropyl)-2,3-dihydro-1-oxo-1H-isoindol-5-yl][(1,2-dihydro-3-methyl-1-oxobenzo[f]quinazolin-9-yl)methyl]amino]carbonyl]oxy]methyl]-5,8-dihydro-5,8-dioxo-1-naphthalenyl]-1,14-dioxo-5,8,11-trioxa-2,15-diazaheptadec-1-yl]-37-(1,14-dioxo-5,8,11-trioxa-2,15-diazadocos-1-yl)-56-hydroxy-1,6,18,22,35,39,53-heptaoxo-,56-oxide, (3S,20S,37S)- (9CI) (CA INDEX NAME)

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H2N----

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RN 341553-47-7 HCAPLUS
10,13,16,26,29,32,35,45,48,51-Decaoxa-2,7,19,23,42,54-hexaaza-58phosphadohexacontane-3,60,62-tricarboxylic acid, 1-[4-[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[(3-carboxy-1-oxopropoxy)methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]phenyl]-22-[17-[6-[[[[1-[5-(5-carboxy-3-methyl-2-pentenyl)-1,3-dihydro-6-methoxy-7-methyl-3-oxo-4-isobenzofuranyl]oxy]-2,2,2-trifluoroethyl]amino]carbonyl]oxy]methyl]-5,8-dioxo-1-naphthalenyl]-1,14-dioxo-5,8,11-trioxa-2,15-diazaheptadec-1-yl]-39-(1,14-dioxo-5,8,11-trioxa-2,15-diazadocos-1-yl)-58-hydroxy-1,6,20,24,37,41,55-heptaoxo-,58-oxide, (3S,22S,39S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

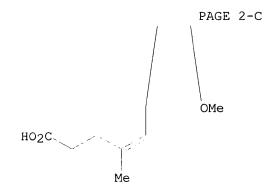
Double bond geometry unknown.

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(CH<sub>2</sub>) 6



RN

341553-59-1 HCAPLUS
Quinolinium, 1-[[[7-[[(21s, 38s)-21-[(16s)-18-[4-[[(2-amino-1, 4-dihydro-4-CN oxo-6-pteridinyl)methyl][[[3-[[(3-carboxy-1-oxopropoxy)methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]p henyl]-16-carboxy-2,13,18-trioxo-6,9-dioxa-3,12,17-triazaoctadec-1-yl]-59,61-dicarboxy-38-(1,14-dioxo-5,8,11-trioxa-2,15-diazadocos-1-yl)-57hydroxy-57-oxido-2,7,20,23,36,40,54-heptaoxo-10,13,16,25,28,31,34,44,47,50decaoxa-3, 6, 19, 22, 37, 41, 53-heptaaza-57-phosphahenhexacont-1-yl]dithio]-8-[(carboxymethyl)dithio]-1,5-dihydro-3-oxido-2,4,3-benzodioxaphosphepin-3yl]oxy]methyl]-4-carboxy-6-fluoro-2-(2'-fluoro-[1,1'-biphenyl]-4-yl)-3methyl-, chloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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RN 341990-94-1 HCAPLUS

L-Alaninamide, N-[41-[2',3'-O-[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[2-oxido-5-(phosphonooxy)-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]methylene]-N-[(4-nitrophenyl)methyl]-5'-thioadenosin-5'-S-yl]-27-[14-[2',3'-O-[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[2-oxido-5-(phosphonooxy)-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]methylene]-N-[(4-nitrophenyl)methyl]-5'-thioadenosin-5'-S-yl]-11-oxo-3,6,9-trioxa-12-azatetradec-1-yl]-1,13,26,38-tetraoxo-12-(11-oxo-3,6,9-trioxa-12-azanonadec-1-yl)-3,6,9,15,18,21,24,30,33,36-decaoxa-12,27,39-triazahentetracont-1-yl]-D-seryl-N-[1-(aminoiminomethyl)-2-hydroxy-3-piperidinyl]- (9CI) (CA INDEX NAME)

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RN 341990-96-3 HCAPLUS

L-Glutamic acid, N-[[5-[2-[2-amino-8-[[[3-[18-[(16S)-18-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[2-oxido-5-(phosphonooxy)-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]methoxy]carbonyl]amino]phenyl]-16-carboxy-13,18-dioxo-3,6,9-trioxa-12,17-diazaoctadec-1-yl]-48-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-33-[15-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-13-oxo-3,6,9-trioxa-12-azapentadec-1-yl]-5,19,32,46-tetraoxo-3,9,12,15,21,24,27,30,36,39,42-undecaoxa-6,18,33,45-tetraazaoctatetracont-1-yl]-4-[[(2R)-2-amino-3-oxo-3-[[(phosphonooxy)methyl]amino]propyl]dithio]phenyl]methoxy]carbonyl]-4,6,7,8-tetrahydro-4-oxo-1H-pyrimido[5,4-b][1,4]thiazin-6-yl]ethyl]-3-thienyl]carbonyl]- (9CI) (CA INDEX NAME)

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341990-98-5 HCAPLUS RN 7,10,13,19,22,25,28,34,37,40-Decaoxa-4,16,31,43-tetraazaoctatetracontan-48-CN oic acid, 47-[[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]][[[3-[[2-(dimethylamino) -2-oxoethoxy] carbonyl] -4-[[5-(phosphonooxy)-2-oxido-1,3,2dioxaphosphorinan-2-yl]oxy]phenyl]methoxy]carbonyl]amino]benzoyl]amino]-31-[17-[5-[[[(2S,3S,4R,5R)-2-(2-amino-4,5-dihydro-4-oxo-1H-pyrrolo[3,2d]pyrimidin-7-y1)-3,4-dihydroxy-5-(2-phosphonoethy1)-1pyrrolidinyl]carbonyl]oxy]methyl]-2-[[(2S)-2-amino-3-oxo-3-[[2-(phosphonooxy)ethyl]amino]propyl]thio]phenyl]-13-oxo-3,6,9,15-tetraoxa-12azaheptadec-1-yl]-1-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-16-[15-[4-[[4-(4chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2Hpyran-2-yl]-13-oxo-3,6,9-trioxa-12-azapentadec-1-yl]-3,17,30,44-tetraoxo-, (47S) - (9CI) (CA INDEX NAME)

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RN 341990-99-6 HCAPLUS
7,10,13,19,22,25,28,34,37,40-Decaoxa-4,16,31,43-tetraazaoctatetracontan-48-oic acid, 47-[[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]][[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[5-(phosphonoxy)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]methoxy]carbonyl]amino]benzoyl]amino]-31-[14-[[3-[[(2R,3R,4S,5S)-5-(2-amino-4,5-dihydro-4-oxo-1H-pyrrolo[3,2-d]pyrimidin-7-yl)-3,4-dihydroxy-2-pyrrolidinyl]methoxy]-8-[(carboxymethyl)dithio]-1,5-dihydro-3-oxido-2,4,3-benzodioxaphosphepin-7-yl]dithio]-13-oxo-3,6,9-trioxa-12-azatetradec-1-yl]-1-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]-2H-pyran-2-yl]-16-[15-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-13-oxo-3,6,9-trioxa-12-azapentadec-1-yl]-3,17,30,44-tetraoxo-, (47S)- (9CI) (CA INDEX NAME)

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RN 341991-00-2 HCAPLUS

Uridine, 5'-O-[7-[[15-[(16S)-18-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[2-oxido-5-(phosphonooxy)-1,3;2-dioxaphosphorinan-2-yl]oxy]phenyl]methoxy]carbonyl]amino]phenyl]-16-carboxy-13,18-dioxo-3,6,9-trioxa-12,17-diazaoctadec-1-yl]-45-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-30-[15-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-13-oxo-3,6,9-trioxa-12-azapentadec-1-yl]-2,16,29,43-tetraoxo-6,9,12,18,21,24,27,33,36,39-decaoxa-3,15,30,42-tetraazapentatetracont-1-yl]dithio]-8-[(carboxymethyl)dithio]-1,5-dihydro-3-oxido-2,4,3-benzodioxaphosphepin-3-yl]-5,6-dihydro-6-oxo-(9CI) (CA INDEX NAME)

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341549-95-9P 341550-24-1P 341550-66-1P
ΙT
     341550-72-9P 341550-74-1P 341550-93-4P
     341550-94-5P 341550-95-6P 341550-97-8P
     341551-63-1P 341551-64-2P 341551-74-4P
     341551-88-0P 341551-93-7P 341552-52-1P
     341552-53-2P 341552-54-3P 341552-96-3P
     341553-21-7P 341553-23-9P 341553-26-2P
     341553-28-4P 341553-29-5P 341553-30-8P
     341553-32-0P 341553-33-1P 341553-36-4P
     341553-43-3P 341553-48-8P 341553-50-2P
     341990-82-7P 341990-83-8P 341990-84-9P
     341990-85-0P 341990-86-1P 341990-87-2P
     341990-95-2P 341990-97-4P
     RL: PNU (Preparation, unclassified); RCT (Reactant); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (multifunctional delivery vehicles for selective cellular targeting of
        drugs)
RN
     341549-95-9 HCAPLUS
     Butanedioic acid, [[5-[[[[(2-amino-1,4-dihydro-4-oxo-6-
CN
     pteridinyl)methyl][4-[(3S)-3-carboxy-33-[2-[[(2R)-10-(9H-fluoren-9-yl)-8-
     (9H-fluoren-9-ylmethoxy)-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-8-
     oxido-3-oxo-7, 9-dioxa-4-aza-8-phosphadec-1-yl]dithio]-5-[[[[[3-[[3-[(9-availar))]]]]]]
     methoxy-5,11-dimethyl-6H-pyrido[4,3-b]carbazol-1-
     yl)amino]propyl]methylamino]propyl]amino]carbonyl]oxy]methyl]phenyl]-
     1,6,29-trioxo-10,13,16,22,25,31-hexaoxa-2,7,19,28-tetraazatritriacont-1-
     yl]phenyl]amino]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-
     yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX
     NAME)
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O CO<sub>2</sub>H

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RN 341550-24-1 HCAPLUS

5,11,14,20,23,26-Hexaoxa-2,8,17,29-tetraazatetratriacontanedioic acid,
33-[[4-[[(7-amino-1,5-dihydro-5-oxopyrido[3,4-b]pyrazin-3-yl)methyl][[[3-[[4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]benzo
yl]amino]-2-[2-[[3-(dimethylamino)-3-oxopropyl]dithio]phenyl]-7,30-dioxo-,
34-(9H-fluoren-9-ylmethyl) 1-[2-oxo-2-[(2S,4S)-2,5,12-tris[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]-1,2,3,4,6,11-hexahydro-7-methoxy-6,11-dioxo-4[[2,3,6-trideoxy-3-(2,3-dihydro-1H-pyrrol-1-yl)-4-O-[(9H-fluoren-9-ylmethoxy)carbonyl]-.alpha.-L-lyxo-hexopyranosyl]oxy]-2naphthacenyl]ethyl] ester (9CI) (CA INDEX NAME)

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NMe2

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RN 341550-66-1 HCAPLUS

CN 5,8-Dioxa-2,11-diazahexadecanedioic acid, 15-[[[5-[2-[2-amino-8-[[[3-[[4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]-4,6,7,8-tetrahydro-4-oxo-1H-pyrimido[5,4-b][1,4]thiazin-6-yl]ethyl]-2-thienyl]carbonyl]amino]-12-oxo-, 1-[[4-[[4-[[4-[[(2S,3S,4R,5R)-2-(2-amino-4,5-dihydro-4-oxo-1H-pyrrolo[3,2-d]pyrimidin-7-yl)-5-[[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]methyl]-3,4-bis[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]-1-pyrrolidinyl]carbonyl]oxy]methyl]phenyl]dithio]-3-[24-carboxy-12-[[(1,1-dioxidobenzo[b]thien-2-yl)methoxy]carbonyl]-5-oxo-3,9,15,18-tetraoxa-21,22-dithia-6,12-diazatetracos-1-yl]phenyl]methyl] 16-(9H-fluoren-9-ylmethyl) ester, (15S)- (9CI) (CA INDEX NAME)

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RN 341550-72-9 HCAPLUS

5,8-Dioxa-2,11-diazahexadecanedioic acid, 15-[[[5-[2-[2-amino-8-[[[3-[[4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]-4,6,7,8-tetrahydro-4-oxo-1H-pyrimido[5,4-b][1,4]thiazin-6-yl]ethyl]-2-thienyl]carbonyl]amino]-12-oxo-, 1-[[4-[[4-[[4-[[(2S,3S,4R,5R)-2-(2-amino-4,5-dihydro-4-oxo-1H-pyrrolo[3,2-d]pyrimidin-7-yl)-5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]methyl]-3,4-bis[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]-1-pyrrolidinyl]carbonyl]oxy]methyl]phenyl]dithio]-3-[2-(carboxymethoxy)ethyl]phenyl]methyl] 16-(9H-fluoren-9-ylmethyl)ester, (15S)- (9CI) (CA INDEX NAME)

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RN 341550-74-1 HCAPLUS

Butanedioic acid, [[5-[[[[2-amino-6-[2-[5-[[[(1S)-4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1-[(9H-fluoren-9-ylmethoxy)carbonyl]-4oxobutyl]amino]carbonyl]-2-thienyl]ethyl]-1,4,6,7-tetrahydro-4-oxo-8H-pyrimido[5,4-b][1,4]thiazin-8-yl]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

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RN 341550-93-4 HCAPLUS

Butanedioic acid, [[5-[[(chlorocarbonyl)oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME) CN

RN 341550-94-5 HCAPLUS
CN Butanedioic acid, [[5-[[[[6-[2-(5-carboxy-2-thienyl)ethyl]-2-[[(1,1-dimethylethyl)diphenylsilyl]amino]-1,4,6,7-tetrahydro-4-oxo-8H-pyrimido[5,4-b][1,4]thiazin-8-yl]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

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RN 341550-95-6 HCAPLUS

CN

Butanedioic acid, [[5-[[[[2-amino-6-[2-(5-carboxy-2-thienyl)ethyl]-1,4,6,7-tetrahydro-4-oxo-8H-pyrimido[5,4-b][1,4]thiazin-8-yl]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

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RN 341550-97-8 HCAPLUS

CN L-Glutamic acid, N-[[5-[2-[2-amino-8-[[[3-[[[4-(9H-fluoren-9-ylmethoxy)1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2yl)oxy]phenyl]methoxy]carbonyl]-4,6,7,8-tetrahydro-4-oxo-1H-pyrimido[5,4b][1,4]thiazin-6-yl]ethyl]-2-thienyl]carbonyl]-, 1-(9H-fluoren-9-ylmethyl)
ester (9CI) (CA INDEX NAME)

RN 341551-63-1 HCAPLUS
CN Butanedioic acid, 9H-fluoren-9-ylmethyl [[5-(hydroxymethyl)-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl ester (9CI) (CA INDEX NAME)

RN 341551-64-2 HCAPLUS

CN Butanedioic acid, 9H-fluoren-9-ylmethyl [[5-formyl-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl ester (9CI) (CA INDEX NAME)

RN 341551-74-4 HCAPLUS

CN L-Glutamic acid, N-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]benzoyl]-, 1-(9H-fluoren-9-ylmethyl) ester (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 341551-88-0 HCAPLUS

CN 3,6,10,15-Tetraoxa-7,9-diphosphaoctadecanoic acid, 7-[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]-14-(2,2-dimethyl-1-oxopropoxy)-13,17,17-trimethyl-16-oxo-9-[2-[(trifluoroacetyl)amino]ethoxy]-, 7,9-dioxide (9CI) (CA INDEX NAME)

RN 341551-93-7 HCAPLUS

CN Benzoic acid, 5-(hydroxymethyl)-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)

RN 341552-52-1 HCAPLUS

CN Benzoic acid, 5-[[(chlorocarbonyl)oxy]methyl]-2-[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)

RN 341552-53-2 HCAPLUS

CN Benzoic acid, 2-[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-5-(hydroxymethyl)-, 2-(dimethylamino)-2-

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oxoethyl ester (9CI) (CA INDEX NAME)

RN 341552-54-3 HCAPLUS

CN Benzoic acid, 2-[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-5-formyl-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)

RN 341552-96-3 HCAPLUS

CN

11,14,17,27,30,33,36,46,49,52-Decaoxa-2,7,20,24,39,43,55-heptaaza-59-phosphatrihexacontane-3,61,63-tricarboxylic acid, 1-[4-[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[[4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]phenyl]-23-(13-carboxy-1-oxo-5,8,11-trioxa-2-azatridec-1-yl)-40-(1,14-dioxo-5,8,11-trioxa-2,15-diazanonadec-1-yl)-59-(9H-fluoren-9-ylmethoxy)-1,6,21,25,38,42,56-heptaoxo-,3,61,63-tris(9H-fluoren-9-ylmethyl) ester, 59-oxide, (3S,23S,40S)-(9CI) (CA INDEX NAME)

PAGE 1-B

NHBu-n

PAGE 1-D

PAGE 2-E

RN 341553-21-7 HCAPLUS
CN 2,4,10-Trioxa-7,12-diaza-3-phosphatridecan-13-oic acid,
7-[6-[[2-(2-aminoethoxy)ethyl][2-[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]ethyl]amino]-4,8-di-1-piperidinylpyrimido[5,4-d]pyrimidin-2-yl]-1-(9H-fluoren-9-yl)-3-(9H-fluoren-9-ylmethoxy)-11-(trifluoromethyl)-, [4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-

# Sackey 09/937386 Page 86

oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[[2-(dimethylamino)-2oxoethoxy]carbonyl]phenyl]methyl ester, 3-oxide (9CI) (CA INDEX NAME)

#### PAGE 1-A

### PAGE 1-B

RN 341553-23-9 HCAPLUS

CN Benzoic acid, 2-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-5-[[[(1-chloro-2,2,2trifluoroethyl)amino]carbonyl]oxy]methyl]-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)

RN 341553-26-2 HCAPLUS

CN 1H-1,4-Diazepinium, 1-[3-[[4-[2-(2-aminoethoxy)ethoxy]-3,5-dimethoxybenzoyl]amino]propyl]-1-[[1-[[[4-[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[(3-methyl-2-oxobutoxy)carbonyl]phenyl]methoxy]carbonyl]amino]-2,2,2-trifluoroethoxy]methyl]hexahydro-4-[4-[(3,4,5-trimethoxybenzoyl)amino]butyl]- (9CI) (CA INDEX NAME)

## PAGE 1-B

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RN 341553-28-4 HCAPLUS

CN Benzoic acid, 2-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-5-[[[[(2,2,2-trifluoro-1hydroxyethyl)amino]carbonyl]oxy]methyl]-, 3-methyl-2-oxobutyl ester (9CI) (CA INDEX NAME)

RN 341553-29-5 HCAPLUS

CN 1H-1,4-Diazepinium, 1-[[1-[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[(3-methyl-2-oxobutoxy)carbonyl]phenyl]methoxy]carbonyl]amino]-2,2,2-trifluoroethoxy]methyl]hexahydro-4-(trifluoroacetyl)-1-[3-[(trifluoroacetyl)amino]propyl]- (9CI) (CA INDEX NAME)

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RN 341553-30-8 HCAPLUS

CN 1H-1,4-Diazepinium, 1-(3-aminopropyl)-1-[[1-[[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[(3-methyl-2-oxobutoxy)carbonyl]phenyl]methoxy]carbonyl]amino]-2,2,2-trifluoroethoxy]methyl]hexahydro- (9CI) (CA INDEX NAME)

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RN 341553-32-0 HCAPLUS

1H-1,4-Diazepinium, 1-[[1-[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[(3-methyl-2-oxobutoxy)carbonyl]methoxy]carbonyl]amino]-2,2,2-trifluoroethoxy]methyl]-1-[3-[[3,5-dimethoxy-4-[2-[2-[[(2-propenyloxy)carbonyl]amino]ethoxy]ethoxy]benzoyl]amino]propyl]hexahydro-(9CI) (CA INDEX NAME)

PAGE 2-B

OMe

RN 341553-33-1 HCAPLUS

1H-1,4-Diazepinium, 1-[[1-[[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[(3-methyl-2-oxobutoxy)carbonyl]phenyl]methoxy]carbonyl]amino]-2,2,2-trifluoroethoxy]methyl]-1-[3-[[3,5-dimethoxy-4-[2-[2-[[(2-propenyloxy)carbonyl]amino]ethoxy]ethoxy]benzoyl]amino]propyl]hexahydro-4-[3-[(3,4,5-trimethoxybenzoyl)amino]propyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

$$\begin{array}{c} \text{MeO} \\ \text{H}_2\text{C} = \text{CH} - \text{CH}_2 - \text{O} - \text{C} - \text{NH} - \text{CH}_2 - \text{CH}_2 - \text{O} - \text{CH}_2 \\ || \\ \text{O} \end{array}$$

PAGE 2-B

RN 341553-36-4 HCAPLUS

CN Butanedioic acid, mono[[[5-[[[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][4-[(3S)-36-[5-[[[[[(2,4-diamino-5-methyl-6-quinazolinyl)methyl](3,4,5-trimethoxyphenyl)amino]carbonyl]oxy]methyl]-2-[[(2R)-10-(9H-fluoren-9-yl)-8-(9H-fluoren-9-ylmethoxy)-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-8-oxido-3-oxo-7,9-dioxa-4-aza-8-phosphadec-1-

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yl]dithio]phenyl]-3-[(9H-fluoren-9-ylmethoxy)carbonyl]-1,6,32-trioxo-10,13,16,22,25,28,34-heptaoxa-2,7,19,31-tetraazahexatriacont-1-yl]phenyl]amino]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl] ester (9CI) (CA INDEX NAME)

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#### PAGE 2-A

PAGE 4-A

PAGE 5-A

PAGE 6-A

PAGE 6-B

- CH<sub>2</sub>- CO<sub>2</sub>H

RN 341553-43-3 HCAPLUS

CN Benzoic acid, 2-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-5-[[(chlorocarbonyl)oxy]methyl]-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)

RN 341553-48-8 HCAPLUS

Butanedioic acid, [[5-[[[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][4-[(3S,19S)-19-amino-3-[(9H-fluoren-9-ylmethoxy)carbonyl]-36-[6-[[[[[1-[[5-[6-(9H-fluoren-9-ylmethoxy)-3-methyl-6-oxo-2-hexenyl]-1,3-dihydro-6-methoxy-7-methyl-3-oxo-4-isobenzofuranyl]oxy]-2,2,2-trifluoroethyl]amino]carbonyl]oxy]methyl]-5,8-dihydro-5,8-dioxo-1-naphthalenyl]-1,6,17,20,33-pentaoxo-10,13,24,27,30-pentaoxa-2,7,16,21,34-pentaazahexatriacont-1-yl]phenyl]amino]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl
9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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PAGE 2-B

PAGE 2-A

RN 341553-50-2 HCAPLUS

8,11-Dioxa-1,5,14,19-tetraazaeicosane-1,2,18-tricarboxylic acid,
20-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[[(4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]phenyl]-4,15,20-trioxo-, 1-(1-[1,1'-biphenyl]-4-yl-1-methylethyl) 18-(9H-fluoren-9-ylmethyl) ester, (2S,18S)- (9CI) (CA INDEX NAME)

PAGE 1-C

PAGE 2-A

RN 341990-82-7 HCAPLUS

CN L-Phenylalanine, N-[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]phenyl]methoxy]carbonyl]-N-[[(4-methoxyphenyl)amino]carbonyl]-L-methionyl-L-leucyl- (9CI) (CA INDEX NAME)

## PAGE 2-A

RN 341990-83-8 HCAPLUS

CN L-Phenylalanine, N-[[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]phenyl]methoxy]carbonyl]-N-[[(4-methoxyphenyl)amino]carbonyl]-L-methionyl-L-leucyl-, 2,2,2-trichloroethylester (9CI) (CA INDEX NAME)

PAGE 1-A

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RN 341990-84-9 HCAPLUS

CN L-Phenylalanine, N-[[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]methoxy]carbonyl]-N-[[(4-methoxyphenyl)amino]carbonyl]-L-methionyl-L-leucyl-, 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

RN 341990-85-0 HCAPLUS

CN Benzoic acid, 5-[[[[[(1S)-1-carboxy-3-(methylthio)propyl][[(4-methoxyphenyl)amino]carbonyl]amino]carbonyl]oxy]methyl]-2-[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-, 1-[2-(dimethylamino)-2-oxoethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 341990-86-1 HCAPLUS

CN Benzoic acid, 5-[[[[(1S)-1-[(1-[1,1'-biphenyl]-4-yl-1-methylethoxy)carbonyl]-3-(methylthio)propyl][[(4-methoxyphenyl)amino]carbonyl]amino]carbonyl]oxy]methyl]-2-[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)

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RN 341990-87-2 HCAPLUS

Benzoic acid, 5-[[[[(1S)-1-[(1-[1,1'-biphenyl]-4-yl-1-methylethoxy)carbonyl]-3-(methylthio)propyl]amino]carbonyl]oxy]methyl]-2-[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 341990-95-2 HCAPLUS

CN Adenosine, 5'-S-(2-aminoethyl)-2',3'-O-[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]phenyl]methylene]-N-[(4-nitrophenyl)methyl]-5'-thio-(9CI) (CA INDEX NAME)

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PAGE 2-A

RN 341990-97-4 HCAPLUS

CN L-Glutamic acid, N-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[4-[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]phenyl]methoxy]carbonyl]amino]benzoyl]-, 1-(9H-fluoren-9-ylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

## IT 341549-55-1P

RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (multifunctional delivery vehicles for selective cellular targeting of drugs)

RN 341549-55-1 HCAPLUS

CN L-Glutamic acid, N-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[[[4-(9H-fluoren-9-ylmethoxy)-1,4-dioxobutoxy]methoxy]carbonyl]-4-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]phenyl]methoxy]carbonyl]amino]benzoyl]-, 1-(9H-fluoren-9-ylmethyl)ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

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L24 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2003 ACS
     2001:185764 HCAPLUS
AN
DN
     134:237345
     Preparation of prodrugs for liver specific drug delivery
ΤI
     Erion, Mark D.; Reddy, K. Raja
PA
     Metabasis Therapeutics, Inc., USA
     PCT Int. Appl., 160 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
     ICM C07F009-6584
IC
     ICS C07F009-6571; C07H015-26; C07H015-252; A61K031-66; A61K031-70;
           A61P031-00; A61P035-00
     26-1 (Biomolecules and Their Synthetic Analogs)
     Section cross-reference(s): 1, 9, 63
FAN.CNT 1
                                                 APPLICATION NO. DATE
     PATENT NO.
                         KIND DATE
PΙ
     WO 2001018013
                         A1
                                20010315
                                                 WO 2000-US24693 20000908
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
               SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
               ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
               DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
               CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                               EP 2000-961694 20000908
     EP 1210354
                          A1
                              20020605
              AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO, MK, CY, AL
PRAI US 1999-153128P P
                                19990908
                                20000908
     WO 2000-US24693
                         W
OS
     MARPAT 134:237345
GΙ
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AΒ Cyclic phosph(oramid)ate prodrugs, such as I [M = pharmaceutical agent, such as camptothecin, paclitaxel, etc.; V, W, W' = H, alkyl, arylalkyl, aryl, heteroaryl, alkenyl, alkynyl, etc.; Z = H, hydroxymethyl, acyloxymethyl, etc.; VZ or VW = fused cyclic group; Y = VZ or VW = VZ or VZ or VW = VZ or H, alkyl, etc.], were prepd. and formulated for pharmaceutical use for the delivery of drugs. Thus, prodrug II was prepd. in 48% yield from 1-(4-pyridyl)-1,3-propanediol, POCl3, and etoposide. The prepd. prodrugs were tested for their resp. biol. activities, such as II being tested for activation in rat hepatocytes. The proposed uses of the prodrugs are to treat diseases that benefit from enhanced drug distribution to the liver and like tissues and cells that express cytochrome P 450, including hepatitis, cancer, liver fibrosis, malaria, other viral and parasitic infections, and metabolic diseases where the liver is responsible for the overprodn. of the biochem. end product, e.g. glucose (diabetes); cholesterol, fatty acids and triglycerides (hyperlipidemia) (atherosclerosis) (obesity). These prodrugs are designed to enhance oral drug delivery, to prolong pharmacodynamic half-life of the drug, to achieve sustained delivery of the parent drug, to increase the therapeutic index of the drug, and to be useful in the delivery of diagnostic imaging agents to the liver.

ST cyclic phosphate prodrug prepn; phosphoramide cyclic prodrug prepn; liver treatment cyclic phosphate prodrug prepn

Drug delivery systems ΙT

(prodrugs; prepn. of prodrugs for liver specific drug delivery)

329325-43-1P **329325-44-2P** IT 329325-41-9P

> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of prodrugs for liver specific drug delivery)

104-55-2 IΤ 2629-72-3, 4-Pyridinepropanol 4704-94-3 4799-68-2 50409-12-6 104196-23-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of prodrugs for liver specific drug delivery)

329325-40-8P, 1-(4-Pyridyl)-1,3-propanediol IT 19790-60-4P 90533-81-6P 329325-45-3P 329325-46-4P 329325-47-5P 329325-42-0P 329361-60-6P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of prodrugs for liver specific drug delivery)

IT 1404-00-8, Mitomycin 7689-03-4, Camptothecin 9014-02-2,

```
11033-22-0, Coformycin 20830-81-3, Daunorubicin
    Neocarzinostatin
    24280-93-1, Mycophenolic acid 25316-40-9, Doxorubicin hydrochloride
                                                     33419-42-0, Etoposide
    29767-20-2, Teniposide 33069-62-4, Paclitaxel
    53910-25-1, Deoxycoformycin 56420-45-2, Epirubicin 58957-92-9,
    Idarubicin 65271-80-9, Mitoxantrone 70052-12-9, Eflornithine
                                                       91421-43-1,
    72496-41-4, Pirarubicin
                             88303-60-0, Losoxantrone
                          91441-23-5, Piroxantrone 97682-44-5, Irinotecan
    9-Aminocamptothecin
    105760-98-3, NK 611 114797-28-3, Esperamicin 114977-28-5, Docetaxel
    117048-59-6, Combretastatin A-4 123948-87-8, Topotecan 127882-73-9, GL
          129564-92-7, Azatoxin 149882-10-0, Lurtotecan 155233-45-7
                            213313-16-7, Combretastatin A-4 (S,S)-dioxolane
    169869-90-3, DX 8951F
    RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT
     (Reactant or reagent); USES (Uses)
        (prepn. of prodrugs for liver specific drug delivery)
             THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
(1) Bedford, S; Bioorganic & Medicinal Chemistry Letters 1996, V6(2), P157
    HCAPLUS
(2) Bristol-Myers Squibb Co; EP 0481214 A 1992 HCAPLUS
(3) Metabasis Therapeutics; WO 9839342 A 1998 HCAPLUS
(4) Metabasis Therapeutics; WO 9839343 A 1998 HCAPLUS
(5) Metabasis Therapeutics; WO 9839344 A 1998 HCAPLUS
(6) Metabasis Therapeutics; WO 9945016 A 1999 HCAPLUS
     329325-41-9P 329325-44-2P
ΙT
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of prodrugs for liver specific drug delivery)
     329325-41-9 HCAPLUS
     Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5-[3,5-dimethoxy-4-
CN
     [[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]-9-[[4,6-
     O-(1R)-ethylidene-.beta.-D-glucopyranosyl]oxy]-5,8,8a,9-tetrahydro-,
     (5R, 5aR, 8aR, 9S) - (9CI) (CA INDEX NAME)
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PAGE 2-A

RN 329325-44-2 HCAPLUS CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-4-[[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]oxy]-, (4S)- (9CI) (CA INDEX NAME)

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ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2003 ACS
T.24
ΑN
     2000:706969 HCAPLUS
     133:261536
DN
     Pharmaceutical compositions comprising cyclic glycerophosphates and
ΤI
     analogs thereof for promoting neural cell differentiation
IN
     Shinitzky, Meir
     Yeda Research and Development Co. Ltd., Israel
PA
     PCT Int. Appl., 42 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
     ICM A61K031-00
IC
     1-11 (Pharmacology)
CC
     Section cross-reference(s): 29, 63
FAN.CNT 1
                                           APPLICATION NO.
                                                             DATE
                      KIND DATE
     PATENT NO.
                            _____
                      ____
                                                             20000324
                            20001005
                                           WO 2000-IL185
     WO 2000057865
                       A2
                            20010628
                      A3
     WO 2000057865
            RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                          BR 2000-9296
                                                             20000324
                            20011218
     BR 2000009296
                       Α
                                                             20000324
                                           EP 2000-912877
                       Α2
                            20011219
     EP 1162959
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
                                            JP 2000-607616
                                                             20000324
     JP 2002540146
                             20021126
                       Т2
PRAI IL 1999-129178
                       Α
                             19990325
                             20000324
     WO 2000-IL185
                       W
     MARPAT 133:261536
OS
     Cyclic glycerophosphates and analogs thereof (CGs) are shown to exert
     neural promoting activities in target cells. Such activities include promotion of neuronal outgrowth, promotion of nerve growth, provision of
     dopaminotrophic supporting environment in a diseased portion of the brain,
     prevention of nerve degeneration and nerve rescue. These activities of
     the CGs render them useful for treatment of various disorders including
     but not limited to mental disorders such as, for example, schizophrenia,
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dementia or disorders resulting in learning disabilities. In addn., these CGs may be used for the treatment of neurodegenerative conditions such as Alzheimer's disease, Parkinson's disease, conditions resulting from exposure to harmful environmental factors or resulting from a mech. injury. The CGs may also be used to treat an individual suffering from a primary neurodegenerative condition in order to prevent or reduce the appearance of secondary degeneration in addnl. nerves ("nerve rescue"). For example, neural outgrowth of PC12 cells was seen when cells were grown in the presence of nerve growth factor (50 ng/mL) or 1,3-cyclic glycerophosphate (1 .mu.M), but not in the presence of linear .alpha.-glycerophosphate.

- ST cyclic glycerophosphate neuronal differentiation mental disorder; antipsychotic schizophrenia cyclic glycerophosphate; Alzheimer disease parkinsonism cyclic glycerophosphate
- Anti-Alzheimer's agents
  Antiparkinsonian agents
  Antipsychotics
  Mental disorder
  Nervous system agents
  Schizophrenia

(compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

IT Monoamines
 Neurotrophic factors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)

(compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

- IT Nerve (degeneration, prevention of; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)
- IT Nerve (differentiation; compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

- IT Nerve, disease
  (injury, neuronal rescue after; compns. comprising cyclic
  glycerophosphates for promoting neural differentiation for therapeutic
  uses)

```
(osmotic pumps; compns. comprising cyclic glycerophosphates for
        promoting neural differentiation for therapeutic uses)
    Cell proliferation
ΙT
        (promotion of; compns. comprising cyclic glycerophosphates for
        promoting neural differentiation for therapeutic uses)
     Drug delivery systems
IT
        (topical; compns. comprising cyclic glycerophosphates for promoting
        neural differentiation for therapeutic uses)
     298701-05-0P
IT
     RL: BAC (Biological activity or effector, except adverse); BPN
     (Biosynthetic preparation); BSU (Biological study, unclassified); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
     711-07-9P 13507-10-3P 22227-09-4P
ΙT
     118897-32-8P 123406-35-9P 286020-33-5P
     298701-06-1P 298701-08-3P 298701-09-4P
     298701-78-7P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
     51-61-6, Dopamine, biological studies
                                              59-92-7, biological studies
ΙT
                       306-08-1, Homovanillic acid
     102-32-9, DOPAC
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
     9001-86-9, Phospholipase C
IT
     RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
     (Uses)
         (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
     57-55-6, 1,2-Propanediol, reactions 96-26-4, Dihydroxyacetone 504-63-2, 1,3-Propanediol 770-12-7, Phenyl phosphorodichloridate
TT
     819-83-0, Disodium .beta.-glycerophosphate 4799-67-1
                                                              14690-00-7,
                                                26776-70-5, Dihydroxyacetone
                                    22002-87-5
     2-Benzyloxy-1,3-propanediol
     dimer
     RL: RCT (Reactant); RACT (Reactant or reagent)
         (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
ΙT
     187976-16-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP
      (Preparation); RACT (Reactant or reagent)
         (compns. comprising cyclic glycerophosphates for promoting neural
        differentiation for therapeutic uses)
     298701-05-0P
IT
     RL: BAC (Biological activity or effector, except adverse); BPN
      (Biosynthetic preparation); BSU (Biological study, unclassified); SPN
      (Synthetic preparation); THU (Therapeutic use); BIOL
      (Biological study); PREP (Preparation); USES (Uses)
         (compns. comprising cyclic glycerophosphates for promoting neural
         differentiation for therapeutic uses)
      298701-05-0 HCAPLUS
RN
      1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide, barium salt (9CI)
CN
      INDEX NAME)
```

●x Ba

T1 711-07-9P 13507-10-3P 22227-09-4P
118897-32-8P 123406-35-9P 286020-33-5P
298701-06-1P 298701-08-3P 298701-09-4P
298701-78-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
 (compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)
RN 711-07-9 HCAPLUS
CN 1,3,2-Dioxaphosphorinane, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 13507-10-3 HCAPLUS CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 22227-09-4 HCAPLUS CN 1,3,2-Dioxaphospholane, 4-methyl-2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 118897-32-8 HCAPLUS

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

CN 1,3,2-Dioxaphospholane, 2-hydroxy-4-methyl-, 2-oxide, barium salt (9CI) (CA INDEX NAME)

●1/2 Ba

RN 123406-35-9 HCAPLUS

CN 9-Octadecenoic acid (9Z)-, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 286020-33-5 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 298701-06-1 HCAPLUS

CN 1,3,2-Dioxaphospholane-4-methanol, 2-hydroxy-, 2-oxide, barium salt (9CI) (CA INDEX NAME)

●x Ba

RN 298701-08-3 HCAPLUS

CN 1,3,2-Dioxaphospholane-4-methanol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

RN 298701-09-4 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-one, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 298701-78-7 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-one, 2-hydroxy-, 2-oxide, barium salt (9CI) (CA INDEX NAME)

## ●1/2 Ba

IT 187976-16-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)

RN 187976-16-5 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-5-(phenylmethoxy)-, 2-oxide (9CI) (CA INDEX NAME)

L24 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 2000:706968 HCAPLUS

DN 133:261549

applicante

applicant

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Cyclic glycerophosphates and analogs for treatment of malignancies
TΙ
    Shinitzky, Meir
ΙN
     Yeda Research and Development Co. Ltd., Israel
PA
     PCT Int. Appl., 52 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
IC
     ICM A61K031-00
     1-12 (Pharmacology)
CC
     Section cross-reference(s): 2, 29, 63
FAN.CNT 1
                                           APPLICATION NO. DATE
                      KIND DATE
     PATENT NO.
                                           _____
                           _____
                                                             20000324
                                           WO 2000-IL184
     WO 2000057864
                      A2
                            20001005
PΙ
     WO 2000057864
                      A3
                            20010531
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
         W:
             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                       A2 20011219
                                           EP 2000-912876
                                                            20000324
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
                                           JP 2000-607615
                                                             20000324
                            20021126
                      Т2
     JP 2002540145
                            19990325
PRAI IL 1999-129179
                       Α
                            20000324
                       W
     WO 2000-IL184
     MARPAT 133:261549
     Cyclic glycerophosphates as well as some analogs thereof (CGs) are shown
     to increase phosphorylation of intracellular proteins in various cells.
     Such activity is not found with linear .alpha. - or .beta. -
     glycerophosphates. The phosphorylating activity of the CGs render them
     useful in the prevention and treatment of various disorders and diseases
     such as, for example, different kinds of malignancies as well as disorders
     involving hormone and hormone-like signaling. The CGs are also useful for
     promotion of target cell differentiation and for detection of abnormal
     conditions in target cells. For example, CHO cells were incubated with 1
     or 2 .mu.M of 1,3-cyclic propanediol phosphate for 1, 3, 5, and 10 min at
     37.degree.. The level of tyrosine phosphorylated proteins in the cell was
     detd. using monoclonal anti-phosphotyrosine antibodies. Phosphorylation
     was most markedly seen in the band(s) having a mol. wt. of .apprx. 35 and
     45 kilodalton.
     cyclic glycerophosphate protein phosphorylation cell differentiation;
ST
     antitumor cyclic glycerophosphate protein phosphorylation; antidiabetic
     cyclic glycerophosphate protein phosphorylation; hormone signaling
     phosphorylation cyclic glycerophosphate therapy
     Antidiabetic agents
IT
     Antitumor agents
     Cytotoxic agents
     Drug delivery systems
         (cyclic glycerophosphates for treatment of malignancies and disorders
         involving hormone-related signaling)
     Hormones, animal, biological studies
TΤ
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
         (cyclic glycerophosphates for treatment of malignancies and disorders
         involving hormone-related signaling)
      Phosphatidylglycerols
IT
```

involving hormone-related signaling)

711-07-9P 13507-10-3P 22227-09-4P ΙT 118897-32-8P 123406-35-9P 286020-33-5P 298701-06-1P 298701-08-3P 298701-09-4P 298701-78-7P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

12629-01-5, Human growth hormone 9004-10-8, Insulin, biological studies IT 62229-50-9, Epidermal growth factor RL: BSU (Biological study, unclassified); BIOL (Biological study)

(cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

IT 9001-86-9, Phospholipase C

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

57-55-6, 1,2-Propanediol, reactions 96-26-4, Dihydroxyacetone 504-63-2, 1,3-Propanediol 770-12-7, Phenyl phosphorodichloridate 819-83-0, Disodium .beta.-glycerophosphate 4799-67-1 14690-00-7, 2-Benzyloxy-1,3-propanediol 22002-87-5 26776-70-5, Dihydroxyacetone dimer

RL: RCT (Reactant); RACT (Reactant or reagent) (cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

IT 187976-16-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

IT 9013-05-2, Phosphatase 9025-82-5, Phosphodiesterase 9026-43-1, Protein kinase 106283-10-7, Inositol 1,4,5-trisphosphate kinase 137632-08-7, ERK 2 kinase 139691-76-2, Raf-1 kinase 142805-58-1, MAPK kinase 155215-87-5, JNK kinase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(protein phosphorylating activity of cyclic glycerophosphates useful for treatment of malignancies and disorders involving hormone-related signaling)

IT 298701-05-0P

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

RN 298701-05-0 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide, barium salt (9CI) (CA INDEX NAME)

●x Ba

TT 711-07-9P 13507-10-3P 22227-09-4P 118897-32-8P 123406-35-9P 286020-33-5P 298701-06-1P 298701-08-3P 298701-09-4P 298701-78-7P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN

(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES

(Uses)

(cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

RN 711-07-9 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 13507-10-3 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 22227-09-4 HCAPLUS

CN 1,3,2-Dioxaphospholane, 4-methyl-2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 118897-32-8 HCAPLUS

CN 1,3,2-Dioxaphospholane, 2-hydroxy-4-methyl-, 2-oxide, barium salt (9CI) (CA INDEX NAME)

●1/2 Ba

RN 123406-35-9 HCAPLUS

CN 9-Octadecenoic acid (9Z)-, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

286020-33-5 HCAPLUS RN

1,3,2-Dioxaphosphorinan-5-ol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME) CN

RN 298701-06-1 HCAPLUS

1,3,2-Dioxaphospholane-4-methanol, 2-hydroxy-, 2-oxide, barium salt (9CI) CN (CA INDEX NAME)

●x Ba

298701-08-3 HCAPLUS RN

1,3,2-Dioxaphospholane-4-methanol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX CN NAME)

298701-09-4 HCAPLUS RN

1,3,2-Dioxaphosphorinan-5-one, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME) CN

RN 298701-78-7 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-one, 2-hydroxy-, 2-oxide, barium salt (9CI) (CA INDEX NAME)

## ●1/2 Ba

IT 187976-16-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

RN 187976-16-5 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-5-(phenylmethoxy)-, 2-oxide (9CI) (CA INDEX NAME)

L24 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 2000:672262 HCAPLUS

DN 134:183352

TI New biodegradable polymer for drug delivery system poly(D,L-lactide-co-ethyl ethylene phosphate)

AU Wen, J.; Kim, G. J. A.; Mao, H. Q.; Zhuo, R. X.; Leong, K. W.

CS Department of Biomedical Engineering, School of Medicine, Johns Hopkins University, Baltimore, MD, 21205, USA

SO Proceedings of the International Symposium on Controlled Release of Bioactive Materials (2000), 27th, 664-665 CODEN: PCRMEY; ISSN: 1022-0178

PB Controlled Release Society, Inc.

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

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Section cross-reference(s): 35
     A copolymer of lactide and Et ethylene phosphate was prepd. and had higher
AΒ
     degrdn. rate, linear degrdn profile, and soly. in nonchlorinated solvents.
     The polymer was used to microencapsulated idoxuridine.
ST
     lactide Et ethylene phosphate polymer drug delivery
TΤ
     Polymer degradation
        (biodegradable polymer for drug delivery system poly(lactide-co-Et
        ethylene phosphate))
IT
     Polymers, biological studies
     RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (biodegradable; biodegradable polymer for drug delivery system
        poly(lactide-co-Et ethylene phosphate))
ΙT
     Drug delivery systems
        (microcapsules; biodegradable polymer for drug delivery system
        poly(lactide-co-Et ethylene phosphate))
ΙT
     Encapsulation
        (microencapsulation; biodegradable polymer for drug delivery system
        poly(lactide-co-Et ethylene phosphate))
IT
     Polyesters, biological studies
     RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (phosphorus-contg.; biodegradable polymer for drug delivery system
        poly(lactide-co-Et ethylene phosphate))
IT
     54-42-2, Idoxuridine
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
     use); BIOL (Biological study); PROC (Process); USES (Uses)
        (biodegradable polymer for drug delivery system poly(lactide-co-Et
        ethylene phosphate))
ΙT
     326604-67-5P
     RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation)
     ; THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
        (biodegradable polymer for drug delivery system poly(lactide-co-Et
        ethylene phosphate))
RE.CNT
              THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Li, S; Polymer 1998, V39, P5421 HCAPLUS
(2) Mao, H; Encyclopedia of Controlled Drug Delivery 1999
(3) Troev, K; J Polym Sci Polym Chem Ed 1996, V34, P621 HCAPLUS
(4) Wen, J; Polym Int 1998, V47, P503 HCAPLUS
    326604-67-5P
IΤ
     RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation)
     ; THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
        (biodegradable polymer for drug delivery system poly(lactide-co-Et
        ethylene phosphate))
RN
     326604-67-5 HCAPLUS
CN
     1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 2-ethoxy-1,3,2-
     dioxaphospholane 2-oxide (9CI) (CA INDEX NAME)
     CM
     CRN 823-31-4
     CMF C4 H9 O4 P
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CM

CRN 95-96-5 CMF C6 H8 O4

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L24 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2003 ACS
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2000:209680 HCAPLUS

DN 132:256044

Ocular lens comprising urethane bond-containing polysiloxane macromer TI

IN Watanabe, Tsuyoshi; Baba, Masaki

PΑ Menicon Co., Ltd., Japan

SO Eur. Pat. Appl., 38 pp. CODEN: EPXXDW

DT Patent

LA English

IC

ICM C08F008-44 ICS C08F008-40; C08F008-34; G02B001-04

63-7 (Pharmaceuticals)

Section cross-reference(s): 35, 38

FAN.CNT 1

	PATENT NO.				KIND		DATE			APPLICATION NO.					DATE			
PI	ΕP	EP 989138 EP 989138			A2		20000329			EP 1999-118558				19990920				
	ΕP				A.	3	20001025											
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PΤ,
			ΙE,	SI,	LT,	LV,	FI,	RO										
	US	6346594			B1		20020212			US 1999-397674				19990916				
	JΡ	2000	56	A2		20000616			JP 1999-263631				1	19990917				
PRAI	JP 1998-266561			Α		19980921												

AB An ocular lens material comprise a silicone compd. having a zwitterionic quaternary ammonium group. The ocular lens material shows excellent transparency, oxygen permeability, deposit resistance and wettability to tears at the same time. Polysiloxane- polyacrylates were prepd. and grafted with sulfopropylammonium betaine to obtain ocular lenses. Phys. properties of the lenses were studied.

ST ocular lens urethane polysiloxane

Polyurethanes, biological studies Polyurethanes, biological studies

RL: DEV (Device component use); SPN (Synthetic preparation); THU

```
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (acrylic-polysiloxane-; ocular lens comprising urethane bond-contg.
        polysiloxane macromer)
    Polysiloxanes, biological studies
TT
    Polysiloxanes, biological studies
    RL: DEV (Device component use); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (acrylic-polyurethane-; ocular lens comprising urethane bond-contg.
       polysiloxane macromer)
ΙT
    Eyeglass lenses
        (ocular lens comprising urethane bond-contg. polysiloxane macromer)
TΤ
    262369-62-0P
    RL: DEV (Device component use); RCT (Reactant); SPN (Synthetic
    preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
        (ocular lens comprising urethane bond-contg. polysiloxane macromer)
ΙT
     6609-64-9DP, reaction products with acrylic siloxanes
                                                             262369-63-1P
                    262369-65-3P
                                   262369-66-4P
                                                  262369-67-5DP, reaction
     262369-64-2P
    products with chlorodioxaphospholane
                                            262369-67-5P 262369-68-6DP
     , reaction products with acrylic siloxanes 262369-69-7P
     262370-62-7P
    RL: DEV (Device component use); SPN (Synthetic preparation);
    THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (ocular lens comprising urethane bond-contg. polysiloxane macromer)
TΨ
     6609-64-9
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (ocular lens comprising urethane bond-contg. polysiloxane macromer)
IT
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP
     (Preparation); RACT (Reactant or reagent)
        (ocular lens comprising urethane bond-contg. polysiloxane macromer)
    262369-68-6DP, reaction products with acrylic siloxanes
IT
    262369-69-7P
    RL: DEV (Device component use); SPN (Synthetic preparation);
     THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (ocular lens comprising urethane bond-contg. polysiloxane macromer)
     262369-68-6 HCAPLUS
RN
     2-Propenoic acid, 2-methyl-, 1,2-ethanediyl ester, polymer with
CN
     2-(dimethylamino)ethyl 2-methyl-2-propenoate, .alpha.-[1,1-dimethyl-9-oxo-
    11-[1,3,3-trimethyl-5-[[[2-[(2-methyl-1-oxo-2-
    propenyl)oxy]ethoxy]carbonyl]amino]cyclohexyl]-5,8-dioxa-10-aza-1-
     silaundec-1-yl]-.omega.-[[1,1-dimethyl-9-oxo-11-[1,3,3-trimethyl-5-[[[2-
     [(2-methyl-1-oxo-2-propenyl)oxy]ethoxy]carbonyl]amino]cyclohexyl]-5,8-
     dioxa-10-aza-1-silaundec-1-yl]oxy]poly[oxy(dimethylsilylene)],
     2-hydroxyethyl 2-methyl-2-propenoate and 3-[3,3,3-trimethyl-1,1-
    bis[(trimethylsily1)oxy]disiloxanyl]propyl 2-methyl-2-propenoate, compd.
    with 2-methoxy-1,3,2-dioxaphospholane 2-oxide (9CI) (CA INDEX NAME)
     CM
          1
     CRN 2196-04-5
     CMF C3 H7 O4 P
```

CM 2

262369-63-1 CRN

(C16 H38 O5 Si4 . C10 H14 O4 . C8 H15 N O2 . C6 H10 O3 . (C2 H6 O CMF

Si)n C50 H90 N4 O15 Si2)x

CCI PMS

> 3 CM

CRN 262369-61-9

CMF (C2 H6 O Si)n C50 H90 N4 O15 Si2

CCI PMS

PAGE 1-A

PAGE 1-B

CM 4

CRN 17096-07-0 CMF C16 H38 O5 Si4

CM 5

CRN 2867-47-2 CMF C8 H15 N O2

$$\begin{array}{c|c} & \text{O} & \text{CH}_2 \\ & || & || \\ \text{Me}_2 \text{N}^- \text{CH}_2 - \text{CH}_2 - \text{O} - \text{C} - \text{C} - \text{Me} \end{array}$$

CM 6

CRN 868-77-9 CMF C6 H10 O3

CM 7

CRN 97-90-5 CMF C10 H14 O4

RN 262369-69-7 HCAPLUS

2-Propenoic acid, 2-methyl-, 1,2-ethanediyl ester, polymer with 2-(dimethylamino)ethyl 2-methyl-2-propenoate, .alpha.-[1,1-dimethyl-9-oxo-11-[1,3,3-trimethyl-5-[[[2-[(2-methyl-1-oxo-2-propenyl)oxy]ethoxy]carbonyl]amino]cyclohexyl]-5,8-dioxa-10-aza-1-silaundec-1-yl]-.omega.-[[1,1-dimethyl-9-oxo-11-[1,3,3-trimethyl-5-[[[2-[(2-methyl-1-oxo-2-propenyl)oxy]ethoxy]carbonyl]amino]cyclohexyl]-5,8-dioxa-10-aza-1-silaundec-1-yl]oxy]poly[oxy(dimethylsilylene)], N,N-dimethyl-2-propenamide and 3-[3,3,3-trimethyl-1,1-bis[(trimethylsilyl)oxy]disiloxanyl]propyl 2-methyl-2-propenoate, compd. with 2-methoxy-1,3,2-dioxaphospholane 2-oxide (9CI) (CA INDEX NAME)

CM 1

CRN 2196-04-5 CMF C3 H7 O4 P

CM 2

CRN 262369-62-0 CMF (C16 H38 O5 Si4 . C10 H14 O4 . C8 H15 N O2 . C5 H9 N O . (C2 H6 O Si)n C50 H90 N4 O15 Si2)× CCI PMS

CM 3

CRN 262369-61-9 CMF (C2 H6 O Si)n C50 H90 N4 O15 Si2 CCI PMS

PAGE 1-A

PAGE 1-B

PAGE 1-C

CM 4

CRN 17096-07-0 CMF C16 H38 O5 Si4

CM 5

CRN 2867-47-2 CMF C8 H15 N O2

$$\begin{array}{c|c} & \text{O} & \text{CH}_2 \\ \parallel & \parallel \\ \text{Me}_2 \text{N-CH}_2 \text{--} \text{CH}_2 \text{--} \text{O-C-C-Me} \end{array}$$

CM 6

CRN 2680-03-7 CMF C5 H9 N O

$$\begin{array}{c} \text{O} \\ || \\ \text{Me}_2 \text{N} - \text{C} - \text{CH} \longrightarrow \text{CH}_2 \end{array}$$

CM 7

CRN 97-90-5 CMF C10 H14 O4

IT 2196-04-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(ocular lens comprising urethane bond-contg. polysiloxane macromer)

RN 2196-04-5 HCAPLUS

CN 1,3,2-Dioxaphospholane, 2-methoxy-, 2-oxide (9CI) (CA INDEX NAME)

L24 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 2000:133529 HCAPLUS

DN 132:175856

TI Methods using a lysophosphatidic acid receptor agonist for promoting survival of myelin-producing cells

IN Chun, Jerold J. M.; Weiner, Joshua A.; Wickens, Philip L.; Begleiter, Leath E.

PA The Regents of the University of California, USA; Allelix Biopharmaceuticals Inc.

SO PCT Int. Appl., 37 pp. CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-665

ICS A61K031-661; C12N005-08; A61P025-28

CC 1-11 (Pharmacology)

Section cross-reference(s): 29

FAN. CNT 1

FAN.	CNT 1 PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
PI	WO 2000009139 WO 2000009139	A2 A3	20000224 20000518	WO 1999-US18069	19990810		

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AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
            CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
            IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
            MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
            SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                           US 1998-153464
                                                            19980915
                            20001121
     US 6150345
                       Α
                                           AU 1999-54735
                                                            19990810
                            20000306
    AU 9954735
                       A1
                       Ρ
                            19980810
PRAI US 1998-96008P
                       Р
                            19980818
     US 1998-96924P
                      Α
                            19980915
     US 1998-153464
     WO 1999-US18069
                       W
                            19990810
     The invention is in the field of neurobiol., and relates particularly to
AΒ
     methods useful for enhancing the survival of myelin producing cells, in
     particular Schwann cells and oligodendrocytes, and thereby to treating
     diseases of the nervous system involving loss of myelination or aberrant
     myelination. The methodol. of the invention uses a survival-promoting
     amt. of an lysophosphatidic acid (LPA) receptor agonist, e.g. LPA.
     myelin cell survival lysophosphidate receptor agonist; Schwann cell
ST
     survival lysophosphidate receptor agonist; oligodendrocyte survival
     lysophosphidate receptor agonist; myelination disease lysophosphidate
     receptor agonist; nervous system disease lysophosphidate receptor agonist
     G proteins (guanine nucleotide-binding proteins)
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (Gi (adenylate cyclase-inhibiting); lysophosphatidic acid receptor
        agonist for promoting survival of myelin-producing cells)
IT
     Receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (LPA1/VZG-1/edg-2; lysophosphatidic acid receptor agonist for promoting
        survival of myelin-producing cells)
ΙT
     Nerve, disease
        (demyelination; lysophosphatidic acid receptor agonist for promoting
        survival of myelin-producing cells)
     Animal tissue culture
ΙT
     Apoptosis
     Myelination
     Nervous system agents
     Oligodendrocyte
     Schwann cell
     Signal transduction, biological
        (lysophosphatidic acid receptor agonist for promoting survival of
        myelin-producing cells)
ΙT
     Lysophosphatidic acids
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); THU (Therapeutic use);
     BIOL (Biological study); PROC (Process); USES (Uses)
         (lysophosphatidic acid receptor agonist for promoting survival of
        myelin-producing cells)
IT
     Myelin
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
      (Biological study); PROC (Process)
         (lysophosphatidic acid receptor agonist for promoting survival of
        myelin-producing cells)
     Gene, animal
ΙT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
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```
(Biological study); PROC (Process)
        (lysophosphatidic acid receptor; lysophosphatidic acid receptor agonist
        for promoting survival of myelin-producing cells)
     Receptors
ΙT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (lysophosphatidic acid; lysophosphatidic acid receptor agonist for
        promoting survival of myelin-producing cells)
ΙT
     Heregulins
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (neuregulin .beta.; lysophosphatidic acid receptor agonist for
        promoting survival of myelin-producing cells)
     Phosphorylation, biological
TΤ
        (protein; lysophosphatidic acid receptor agonist for promoting survival
        of myelin-producing cells)
     Lysophosphatidic acids
ΙT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (receptors; lysophosphatidic acid receptor agonist for promoting
        survival of myelin-producing cells)
ΙT
     Receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (sphingosine 1-phosphate; lysophosphatidic acid receptor agonist for
        promoting survival of myelin-producing cells)
     Multiple sclerosis
IT
        (therapeutic agents; lysophosphatidic acid receptor agonist for
        promoting survival of myelin-producing cells)
     26993-30-6, Sphingosine 1-phosphate
ΙT
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (lysophosphatidic acid receptor agonist for promoting survival of
        myelin-producing cells)
                                 259225-84-8P
                                                259225-85-9P
     169736-88-3P 259225-83-7P
                                   259231-37-3P
                    259225-87-1P
     259225-86-0P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (lysophosphatidic acid receptor agonist for promoting survival of
        myelin-producing cells)
     65528-98-5
ΙT
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (lysophosphatidic acid receptor agonist for promoting survival of
        myelin-producing cells)
     115926-52-8, Phosphoinositide 3-kinase
                                               149147-12-6, Akt kinase
ΙT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
      (Biological study); PROC (Process)
         (lysophosphatidic acid receptor agonist for promoting survival of
        myelin-producing cells)
                                83258-36-0P
                                              259231-36-2P
IT
     111-58-0P
                 18704-66-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (prepn. and reaction; lysophosphatidic acid receptor agonist for
        promoting survival of myelin-producing cells)
                                                         112-77-6, Oleovl
                            112-16-3, Lauroyl chloride
     87-66-1, Pyrogallol
ΙT
                                       156-87-6, 1-Propanol-3-amine
                 141-43-5, reactions
      chloride
```

1,2,3-Cyclohexanetriol 7719-09-7, Thionyl chloride 7790-94-5,
Chlorosulfuric acid 10025-87-3, Phosphorus oxychloride 25496-72-4,
Monoolein 26402-26-6, Monocaprylin
RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction; lysophosphatidic acid receptor agonist for promoting
 survival of myelin-producing cells)
169736-88-3P 259225-83-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study unclassified): SPN (Synthetic preparation): THU

study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)

(lysophosphatidic acid receptor agonist for promoting survival of myelin-producing cells)

RN 169736-88-3 HCAPLUS

ΙT

CN 9-Octadecenoic acid (9Z)-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HO P R O (CH<sub>2</sub>) 
$$7$$
  $\overline{Z}$  (CH<sub>2</sub>)  $7$  Me

### Na

RN 259225-83-7 HCAPLUS

CN Octanoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt (9CI) (CA INDEX NAME)

### Na

L24 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:576934 HCAPLUS

DN 131:185194

TI Preparation of cyclic nucleotides as FBPase inhibitor prodrugs

IN Erion, Mark D.; Reddy, K. Raja; Robinson, Edward D.

PA Metabasis Therapeutics, Inc., USA

SO PCT Int. Appl., 240 pp.

CODEN: PIXXD2

DT Patent

LA English

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ICM C07H019-00
IC
     33-9 (Carbohydrates)
CC
     Section cross-reference(s): 7, 63
FAN.CNT 2
                                            APPLICATION NO. DATE
     PATENT NO.
                      KIND DATE
                                            _____
                                                              _____
     _____
                      ____
                            _____
                             19990910
                                            WO 1999-US4908
                                                              19990305
                       A2
     WO 9945016
PΙ
                             20000615
     WO 9945016
                       Α3
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             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
             KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
              CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                            CA 1999-2322487 19990305
     CA 2322487
                       AΑ
                             19990910
                                                               19990305
                                             AU 1999-30699
     AU 9930699
                        A1
                             19990920
                                            EP 1999-912300
                                                               19990305
                        A2
                             20001220
     EP 1060182
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, FI
                                             JP 2000-534558
                                                              19990305
     JP 2002505333
                        T2
                             20020219
PRAI US 1998-77164P
                        Ρ
                             19980306
                        Ρ
                             19980306
     US 1998-77165P
                        W
                             19990305
     WO 1999-US4908
     MARPAT 131:185194
OS
GΙ
```

Prodrugs of phosphorus-contg. nucleotides I, wherein V is selected from AΒ the group consisting of H, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -R9; or together V and Z are connected via 3-5 atoms to form a cyclic group, optionally contg. 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or together V and Z are connected via 3-5 atoms to form a cyclic group, optionally contg. 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the oxygen attached to the phosphorus. Together V and W are connected via 3 carbon atoms to form an optionally substituted cyclic group contg. 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; W and R are independently selected from the group consisting of H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -R9. Z is selected from the group consisting of -CHR2OH, -CHR2OC(O)R3, -CHR2OC(S)R3, -CHR2OC(S)OR3, -CHR2OC(O)SR3, -CHR2OCO2R3,

ST

IT

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ΙT

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TT

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-OR2, -SR2, -CHR2N3, -CH2aryl, -CH(aryl)OH, -CH(CH=CR22)OH,
-CH(C.tplbond.CR2)OH, -R2, -NR22, -OCOR3, -OCO2R3, -SCOR3, -SCO2R3,
-NHCOR2, -NHCO2R3, -CH2NHaryl, (CH2)p-OR2, and (CH2)p-SR2; -R2 is an R3 or
-H; R3 is selected from the group consisting of alkyl, aryl, aralkyl, and
alicyclic; and R9 is selected from the group consisting of alkyl, aralkyl,
and alicyclic; p is an integer from 2 to 3. With the proviso that (a) V,
Z, W, and R are not all -H; and (b) when Z is -R2, then at least one of V
and W is not -H, or -R9; and M is selected from the group that attached to
PO32-, P2063-, or P3094- is biol. active in vivo, and that is attached to
the phosphorus in I via a carbon, oxygen, or nitrogen atom; and
pharmaceutically acceptable prodrugs and salts thereof. Thus, cyclic
nucleotide I (M = adenine-9-.beta.-D-arabinofuranos-5'-yl; V = 4-pyridyl;
Z = W = R = H) was prepd. and tested as prodrug human liver FBPase
inhibitor (EC50 < 10 .mu.M).
drug delivery system nucleotide prepn enzyme inhibitor; cyclic nucleotide
prepn enzyme FBPase inhibitor prodrug
Drug delivery systems
   (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
Nucleotides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); IMF (Industrial manufacture); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
   (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
Drug delivery systems
   (prodrugs; prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
180255-38-3
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
   (human liver; prepn. of cyclic nucleotides as FBPase inhibitor
   prodrugs)
                                                          213198-79-9P
              85665-04-9P
                            213125-14-5P
                                           213198-14-2P
59354-01-7P
                                                            213199-10-1P
                                             213199-07-6P
                              213199-00-9P
               213198-98-2P
213198-81-3P
                                             213199-30-5P
                              213199-28-1P
                                                            213199-40-7P
               213199-26-9P
213199-25-8P
                                                            213200-50-1P
                                             213200-07-8P
               213199-70-3P
                              213199-82-7P
213199-58-7P
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                                             213201-33-3P
213200-52-3P
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                                                            213201-44-6P
                              213201-40-2P
213201-37-7P
               213201-38-8P
                                             213201-50-4P
                                                            213201-51-5P
213201-47-9P
               213201-48-0P
                              213201-49-1P
                                             213201-55-9P
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                              213201-54-8P
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                                             240434-10-0P
213247-37-1P
               213247-77-9P
                              213248-32-9P
                                             240434-28-0P
                                                            240434-29-1P
                              240434-27-9P
240434-22-4P
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                                             240434-33-7P
                                                             240434-45-1P
                              240434-32-6P
               240434-31-5P
240434-30-4P
               240434-47-3P
                              240434-49-5P
                                             240434-50-8P
                                                            240434-51-9P
240434-46-2P
240434-52-0P 240434-53-1P 240434-54-2P
240434-55-3P 240434-56-4P 240434-57-5P
240434-58-6P 240434-59-7P 240434-60-0P
240487-26-7P 240487-27-8P 240487-28-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); IMF (Industrial manufacture); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL
 (Biological study); PREP (Preparation); USES (Uses)
    (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
9001-40-5, Glucose-6-phosphate dehydrogenase 9001-78-9
                                                            9016-18-6,
Carboxyesterase
RL: CAT (Catalyst use); USES (Uses)
    (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
                            110-60-1, 1,4-Butanediamine 110-70-3,
78-77-3, Isobutyl bromide
                                                              814-49-3,
                               498-60-2, 3-Furfuraldehyde
N.N'-Dimethylethylene diamine
Diethylchlorophosphate 1826-67-1, Vinylmagnesium bromide
                                                              2627-69-2
2859-68-9, 2-Pyridine propanol 4704-94-3 4799-68-2
                                                        5413-85-4,
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5813-64-9, Neopentylamine
     5-Amino-4,6-dichloropyrimidine
                  50409-12-6
                               65641-62-5
                                          106941-25-7
                                                          213124-94-8
    41368-63-2
    213248-53-4
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
                                               33300-35-5P
                                                            100391-74-0P
     19790-60-4P
                   23274-21-7P
                                 33235-31-3P
IT
                                                  213124-95-9P
                                                                  213201-43-5P
                                   131245-85-7P
     104208-14-2P
                    119901-99-4P
                                                  213248-30-7P
                                                                  213248-31-8P
                                   213201-62-8P
     213201-45-7P
                    213201-61-7P
                                                  240434-21-3P
                                                                  240434-23-5P
                                   213248-52-3P
     213248-46-5P
                    213248-47-6P
                                                                  240434-41-7P
                                   240434-36-0P
                                                  240434-38-2P
     240434-24-6P
                    240434-25-7P
                                   240434-61-1P
                                                  240487-25-6P
     240434-43-9P
                    240434-48-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
     240434-53-1P 240434-54-2P 240434-55-3P
IT
     240434-56-4P 240434-57-5P 240434-58-6P
     240434-59-7P 240434-60-0P 240487-27-8P
     240487-28-9P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); IMF (Industrial manufacture); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (prepn. of cyclic nucleotides as FBPase inhibitor prodrugs)
RN
     240434-53-1 HCAPLUS
     9H-Purin-6-amine, 9-[5-0-(2-oxido-4-phenyl-1,3,2-dioxaphosphorinan-2-yl)-
CN
     .beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.

RN 240434-54-2 HCAPLUS

CN 9H-Purin-6-amine, 9-[5-O-[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 240434-55-3 HCAPLUS

CN 6H-Purin-6-one, 1,9-dihydro-9-[(2R,5S)-tetrahydro-5-[[[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]oxy]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 240434-56-4 HCAPLUS

CN 1H-1,2,4-Triazole-3-carboxamide, 1-[5-0-[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]-.beta.-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 240434-57-5 HCAPLUS

CN 9H-Purin-6-amine, 2-fluoro-9-[5-0-[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 240434-58-6 HCAPLUS

CN 9H-Purin-6-amine, 9-[(2R,5S)-tetrahydro-5-[[[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]oxy]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

RN 240434-59-7 HCAPLUS

CN Uridine, 2'-deoxy-5-fluoro-5'-O-[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 240434-60-0 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-[[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]oxy]ethoxy]methyl]- (9CI) (CA INDEX NAME)

RN 240487-27-8 HCAPLUS

CN 9H-Purin-6-amine, 9-[5-0-[5-[(acetyloxy)methyl]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 240487-28-9 HCAPLUS

CN Uridine, 2'-deoxy-5-fluoro-3',5'-bis-0-[2-oxido-4-(4-pyridinyl)-1,3,2-dioxaphosphorinan-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

- L24 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2003 ACS
- AN 1998:169488 HCAPLUS
- DN 128:257656
- TI Preparation of amphiphilic glycerols or ethyleneglycols as phosphatidylcholine synthesis inhibitors and antitumors
- IN Attard, George Simon; McGuigan, Christopher; Riley, Patrick Anthony
- PA University of Southampton, UK; Attard, George Simon; McGuigan, Christopher; Riley, Patrick Anthony
- SO PCT Int. Appl., 57 pp.
- CODEN: PIXXD2
- DT Patent
- LA English
- IC ICM A61L031-00
- CC 33-6 (Carbohydrates)

Section cross-reference(s): 1

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

```
WO 9809668
                             19980312
                                             WO 1997-GB2410
                                                               19970908
                        Α2
     WO 9809668
                        AЗ
                             19980625
         W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
             US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
     AU 9741285
                       A1
                             19980326
                                             AU 1997-41285
                                                               19970908
PRAI GB 1996-18634
                             19960906
     WO 1997-GB2410
                             19970908
OS
     MARPAT 128:257656
AΒ
     Use of an amphiphilic compd. in the manuf. of a medicament for the
     inhibition of phosphatidylcholine synthesis, said amphiphilic compd. have
     the following properties: (i) the compd. comprises a non-ionic, cationic
     or anionic hydrophilic head group and a hydrophobic tail group; (ii) the
     head group has a cross section A and the tail group has a cross section B
     such that the ratio B:A is less than 0.7:1; (iii) the tail group comprises
     a straight hydrocarbon chain having from 8 to 18 carbon atoms; and i.v.
     the amphiphilic compd. has a membrane/water partition coeff. of more than
     1 \times 10^{-3}. Thus, 1-0-(5',5'-dimethyl-1',3'-dioxa-2'-phosphacyclohexane-2'-
     oxide)-2-0-methyl-3-0-hexadecyl-rac-glycerol was prepd. and tested for its
     antitumor and hemolytic activity (HC50 \approx 0.044-0.178).
ST
     hemolytic activity phosphatidylcholine inhibitor antitumor; ethyleneglycol
     amphiphilic prepn phosphatidylcholine inhibitor antitumor; amphiphilic
     glycerol prepn phosphatidylcholine inhibitor antitumor
IT
     Antitumor agents
        (prepn. of amphiphilic glycerols or ethyleneglycols as
        phosphatidylcholines synthesis inhibitors and antitumors)
ΤT
     Phosphatidylcholines, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (prepn. of amphiphilic glycerols or ethyleneglycols as
        phosphatidylcholines synthesis inhibitors and antitumors)
ΙT
     Amphiphiles
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of amphiphilic glycerols or ethyleneglycols as
        phosphatidylcholines synthesis inhibitors and antitumors)
ΙT
     Glycols, preparation
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of amphiphilic glycerols or ethyleneglycols as
        phosphatidylcholines synthesis inhibitors and antitumors)
IT
     57-09-0P
                1119-97-7P
                             3055-98-9P
                                           5698-39-5P
                                                         13149-87-6P
                                                 29908-17-6P 194147-98-3P
     15590-96-2P
                    24233-81-6P
                                  27847-86-5P
     204924-40-3P 204924-42-5P 204924-43-6P
     204924-44-7P
                     204924-45-8P
                                    204924-47-0P 204924-48-1P
     204924-50-5P 204924-52-7P
                                  204924-53-8P
                                                  204924-56-1P
     204924-58-3P
                     204924-59-4P
                                    204924-60-7P
                                                    204924-61-8P
                                                                    204924-62-9P
                     205132-42-9P, Mitelfosine
     204924-79-8P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of amphiphilic glycerols or ethyleneglycols as
        phosphatidylcholines synthesis inhibitors and antitumors)
IΤ
     100-79-8, Solketal
                           143-15-7, 1-Bromododecane 626-67-5, N-Methyl
```

piperidine

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of amphiphilic glycerols or ethyleneglycols as phosphatidylcholines synthesis inhibitors and antitumors)

ΙT 112-82-3P, 1-Bromohexadecane 140-72-7P 6145-69-3P 7252-87-1P 14847-87-1P 36324-72-8P 41672-91-7P 10395-09-2P 71221-96-0P

82002-20-8P 84337-41-7P 162758-12-5P 162870-36-2P 194147-97-2P

204924-74-3P 204924-77-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of amphiphilic glycerols or ethyleneglycols as phosphatidylcholines synthesis inhibitors and antitumors)

IT 194147-98-3P 204924-40-3P 204924-42-5P 204924-43-6P 204924-48-1P 204924-52-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(prepn. of amphiphilic glycerols or ethyleneglycols as phosphatidylcholines synthesis inhibitors and antitumors)

194147-98-3 HCAPLUS RN

CN 1,3,2-Dioxaphosphorinane, 5-dodecyl-2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

204924-40-3 HCAPLUS RN

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-5-tetradecyl-, 2-oxide (9CI) (CA INDEX NAME)

204924-42-5 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 5-hexadecyl-2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 204924-43-6 HCAPLUS

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-5-octadecyl-, 2-oxide (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me}-\text{(CH2)}_{17} \\ \hline \\ \text{O} \\ \\ \text{OH} \end{array}$$

RN 204924-48-1 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-[3-(hexadecyloxy)-2-methoxypropoxy]-, 2-oxide (9CI) (CA INDEX NAME)

RN 204924-52-7 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-[3-(hexadecyloxy)-2-methoxypropoxy]-5,5-dimethyl-, 2-oxide (9CI) (CA INDEX NAME)

L24 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 1997:237764 HCAPLUS

DN 126:220705

TI Tumor metastasis inhibitors containing 1-0-acylglycerol-2,3-phosphates

IN Kobayashi, Susumu; Matsumoto, Myoko; Onimura, Kenjiro; Aketo, Hitoshi; Aragai, Kyoko; Mukai, Michiko

PA Sagami Chem Res, Japan

SO Jpn. Kokai Tokkyo Koho, 11 pp. CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM A61K031-665

ICS C07F009-10; C07F009-6574

CC 1-6 (Pharmacology)

Section cross-reference(s): 33

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE
PI JP 09025235 A2 19970128 JP 1995-177170 19950713
PRAI JP 1995-177170 19950713

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Sackey 09/937386 Page 148
     MARPAT 126:220705
OS
GΙ
   - O ---- COR
                  Ι
     The metastasis inhibitors contain the title compds. I (R = C2-30 linear or
AΒ
     branched alkyl, alkenyl, alkynyl which may contain cycloalkane ring; M =
     H, counter cation) as active ingredients. I (COR = palmitoyl, M = Na)
     (prepn. given) at 25 .mu.M showed >99% inhibition against
     1-O-oleoyllysophosphatidic acid-induced infiltration of rat ascites
     hepatoma cell (MM1) into a cultured monolayer of peritoneal mesothelial
     cells, vs. 96% at 12.5 .mu.M for PHYLPA.
     acylglycerol phosphate prepn metastasis inhibitor; tumor metastasis
ST
     inhibitor acylglycerol phosphate; glycerophospholipid prepn tumor
     metastasis inhibitor
     Antitumor agents
TΤ
        (metastasis; prepn. of 1-O-acylglycerol-2,3-phosphates as tumor
        metastasis inhibitors)
     168217-09-2P 168217-10-5P 169736-88-3P
IT
     188171-56-4P 188171-60-0P 188171-62-2P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
      (Therapeutic use); BIOL (Biological study); PREP
      (Preparation); USES (Uses)
         (prepn. of 1-O-acylglycerol-2,3-phosphates as tumor metastasis
        inhibitors)
                                        112-80-1, 9-Octadecenoic acid (Z)-,
     57-10-3, Palmitic acid, reactions
ΙT
                 373-49-9 506-30-9, Eicosanoic acid
                                                        10030-73-6
     reactions
     89155-39-5, 9-Hexadecynoic acid
      RL: RCT (Reactant); RACT (Reactant or reagent)
         (prepn. of 1-O-acylglycerol-2,3-phosphates as tumor metastasis
         inhibitors)
                                   129784-87-8P
                                                                 188171-53-1P
                    125226-51-9P
                                                  150447-02-2P
 ΙT
      14347-78-5P
                                                                 188171-59-7P
                                                   188171-58-6P
                     188171-55-3P
                                   188171-57-5P
      188171-54-2P
                    188182-87-8P
                                    188182-88-9P
      188171-61-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (prepn. of 1-0-acylglycerol-2,3-phosphates as tumor metastasis
         inhibitors)
      168217-09-2P 168217-10-5P 169736-88-3P
 ΤТ
      188171-56-4P 188171-60-0P 188171-62-2P
      RL: BAC (Biological activity or effector, except adverse); BSU (Biological
      study, unclassified); SPN (Synthetic preparation); THU
      (Therapeutic use); BIOL (Biological study); PREP
      (Preparation); USES (Uses)
         (prepn. of 1-0-acylglycerol-2,3-phosphates as tumor metastasis
         inhibitors)
```

9-Hexadecenoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-

168217-09-2 HCAPLUS

RN

CN

yl]methyl ester, sodium salt, (9Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

Na

RN 168217-10-5 HCAPLUS

CN 9-Hexadecynoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$CH_2$$
 7  $C = C - (CH_2) 5$ 

Na

RN 169736-88-3 HCAPLUS

CN 9-Octadecenoic acid (9Z)-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HO 
$$\stackrel{\text{O}}{=}$$
  $\stackrel{\text{O}}{=}$   $\stackrel{\text{O}}{=}$ 

Na

RN 188171-56-4 HCAPLUS

CN 9-Hexadecenoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (9E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

Na

RN 188171-60-0 HCAPLUS

CN Nonanoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

RN 188171-62-2 HCAPLUS

CN Eicosanoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

L24 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 1997:224038 HCAPLUS

DN 126:212447

TI Phosphorous-containing dipeptide inhibitors of cysteine and serine protease

IN Mallamo, John P.; Bihovsky, Ron; Tao, Ming; Wells, Gregory J.

PA Cephalon, Inc., USA

SO PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DT Patent

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

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T.A
     English
IC
     ICM A61K031-66
          A61K031-665; A61K031-675; C07F009-09; C07F009-32; C07F009-40;
           C07F009-53; C07F009-572; C07F009-6533; C07F009-6574
CC
     34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 1, 7
FAN.CNT 1
     PATENT NO.
                         KIND DATE
                                                 APPLICATION NO.
                                                                   DATE
PΙ
     WO 9703679
                         Α1
                                19970206
                                                 WO 1996-US11625
                                                                    19960712
         W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
               SE, SG
          RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
               IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN
     US 5639732
                                19970617
                                                US 1996-679342
                                                                   19960710
                         Α
     CA 2226414
                                19970206
                                                 CA 1996-2226414 19960712
     AU 9664583
                          A1
                                19970218
                                                 AU 1996-64583
                                                                    19960712
                          A1
                                19981021
                                               EP 1996-923756
                                                                    19960712
     EP 871454
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, FI
                          Т2
                                19990817
                                                 JP 1996-506762
                                                                   19960712
     JP 11509231
                          Ρ
PRAI US 1995-1491P
                                19950717
     US 1996-679342
                          Α
                                19960710
     WO 1996-US11625
                          W
                                19960712
OS
     MARPAT 126:212447
```

$$O | (O) mR^4$$
  
-  $(O) z$   $P$   $O nR^5 I$ 

GΙ

The present invention is directed to novel phosphorous-contg. inhibitors of cysteine or serine proteases of the formula X-W-Y-CH(R2)-CO-NH-CH(R1)-CO-[CH(R3)]t-Q wherein: X=e.g., C6-C14 aryl, heteroaryl with C6-C14 ring atoms, C1-C10 alkyl (un) substituted with one or more J groups, C1-C10 alkoxy; W=C0, S02; Y=NH, (CH2)k where k=0-3; R1 and R2 are independently, e.g., H, C1-C14 alkyl (un) substituted with one or more J groups, C3-C10 cycloalkyl (un) substituted with one or more J groups; R3=e.g., H, lower alkyl, aryl, heteroaryl; t=0 or 1; Q=I wherein m, n, and z are independently 0 or 1; R4 and R5 are independently, e.g., H, lower alkyl (un) substituted with J, heteroaryl (un) substituted with J, or taken together to form a 5-8 membered heterocyclic ring (un) substituted with J; J=e.g., halogen, alkyl, guanidino, alkoxy. Thus, e.g., substitution reaction of Z-Leu-Phe-CH2Br with

II

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bis(phenethyl)phosphate afforded dipeptide deriv. II (Z = PhCH2O2C) in 62%
     yield which exhibited 99% inhibition of calpain I at 0.1 .mu.M. Methods
     for the use of the protease inhibitors are also described.
ST
     dipeptide prepn inhibitor cysteine serine protease; peptide phosphonate
     cysteine serine protease inhibitor; phosphorous contg peptide serine
     protease inhibitor; cysteine protease inhibitor phosphorous contg peptide
TΤ
     Dipeptides
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (phosphono analogs; prepn. of phosphorous-contg. dipeptide inhibitors
        of cysteine and serine protease)
ΙT
     78990-62-2, Calpain
     RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
     (Miscellaneous); BIOL (Biological study); PROC (Process)
        (I; prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and
        serine protease)
TT
     187976-26-7P
                    187976-27-8P
                                    187976-28-9P
                                                   187976-29-0P
                                                                  187976-31-4P
     187976-32-5P
                    187976-33-6P
                                   187976-34-7P
                                                   187976-35-8P
                                                                  187976-36-9P
     187976-37-0P
                    187976-38-1P
                                   187976-39-2P
                                                   187976-40-5P
                                                                  187976-41-6P
     187976-42-7P
                    187976-43-8P
                                    187976-44-9P
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                    187976-48-3P
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                                                                  187976-51-8P
                    187976-53-0P
     187976-52-9P
                                   187976-54-1P
                                                   187976-55-2P
                                                                  187976-56-3P
     187976-57-4P
                    187976-58-5P
                                   187976-59-6P 188010-56-2P
     188013~51-6P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of phosphorous-contq. dipeptide inhibitors of cysteine and
        serine protease)
TΨ
     37259-58-8, Serine protease 37353-41-6, Cysteine protease
     RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
     (Miscellaneous); BIOL (Biological study); PROC (Process)
        (prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and
        serine protease)
     60-12-8, Phenethyl alcohol 103-63-9, (2-Bromoethyl)benzene 10 Dibutyl phosphate 109-70-6, 1-Bromo-3-chloropropane 110-91-8,
IT
                                                                     107-66-4,
                            298-07-7, Bis(2-ethylhexyl) phosphate
     Morpholine, reactions
                                                                       644 - 97 - 3,
     Phenyl dichlorophosphine 677-24-7, Methyl dichlorophosphate
                                                                      813 - 78 - 5,
     Dimethyl phosphate 868-85-9, Dimethyl phosphite
                                                        993-13-5,
     Methylphosphonic acid
                            1571-33-1, Phenylphosphonic acid
                                                                 1623-08-1,
     Dibenzyl phosphate 1809-19-4, Dibutyl phosphite
                                                         2018-66-8,
     N-Benzyloxycarbonyl-leucine
                                  3283-12-3, Dimethylphosphinic acid
     3445-11-2, 1-(2-Hydroxyethyl)-2-pyrrolidinone
                                                      3647-69-6,
     N-(2-Chloroethyl)morpholine hydrochloride
                                                  4552-91-4
     14690-00-7, 2-Benzyloxy-1,3-propanediol
                                                15948-60-4, Bis(4-
     chlorophenyl)phosphine oxide 20434-05-3
                                                  58521-45-2,
     N-tert-Butoxycarbonyl-leucinal
                                       95322-86-4
                                                    110972-27-5,
     N, N-Diisopropylmethylphosphonamidic chloride
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and
        serine protease)
TΨ
     2227-43-2P
                  2511-09-3P, Ethyl phenylphosphinate
                                                         7357-67-7P
     13317-44-7P, Ethyl phenylphosphinic acid
                                                14561-21-8P,
                                                        19236-48-7P
     Bis(2-phenylethyl)phosphinic acid
                                          18593-19-6P
                                                24935-94-2P, Dipentylphosphinic
     19236-58-9P
                   19236-61-4P
                                  20148-17-8P
                                         50972-25-3P
                                                       97785-51-8P
     acid
            31735-80-5P
                          39063-70-2P
     101523-04-0P
                    118252-76-9P
                                   118930-87-3P 151091-71-3P 187975-99-1P
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187976-12-1P 187976-03-0P 187976-05-2P 187976-07-4P 187976-01-8P 187976-20-1P 187976-14-3P **187976-16-5P** 187976-18-7P 187976-25-6P 187976-60-9P 187976-23-4P 187976-24-5P 187976-22-3P 187976-61-0P **187976-62-1P** 187976-63-2P 187976-64**-**3P 187976-69-8P 187976-66-5P 187976-67-6P 187976-68-7P 187976-65-4P 187976-74-5P 187976-72-3P 187976-73-4P 187976-71-2P 187976-70-1P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and serine protease)

IT 57616-74-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and serine protease)

IT 188010-56-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)
 (prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and
 serine protease)

RN 188010-56-2 HCAPLUS

CN Carbamic acid, [3-methyl-1-[[[3-[[2-oxido-5-(phenylmethoxy)-1,3,2-dioxaphosphorinan-2-yl]oxy]-2-oxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester, [2[S(S)]]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 187976-16-5P 187976-62-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(prepn. of phosphorous-contg. dipeptide inhibitors of cysteine and serine protease)

RN 187976-16-5 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-5-(phenylmethoxy)-, 2-oxide (9CI) (CA INDEX NAME)

RN 187976-62-1 HCAPLUS

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Sackey 09/937386 Page 154
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1,3,2-Dioxaphosphorinane, 2-methoxy-5-(phenylmethoxy)-, 2-oxide (9CI) (CA INDEX NAME) Ph-CH2-O L24 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2003 ACS 1996:672866 HCAPLUS AN 125:339157 DN Preparation of lysophosphatidic acids for treating hyperproliferative ΤI conditions Piazza, Gary A.; Mazur, Adam W. ΙN The Procter & Gamble Company, USA PA U.S., US14 pp., Cont. of U. S. Ser. No. 980,814, abandoned. SO CODEN: USXXAM DT Patent LA English ICM A61K031-66 IC 514110000 NCL 63-8 (Pharmaceuticals) CC Section cross-reference(s): 28, 62 FAN.CNT 1 APPLICATION NO. DATE KIND DATE PATENT NO. \_\_\_\_\_ \_\_\_\_ US 1994-334888 19941104 19961015 US 5565439 19921124 PRAI US 1992-980814 MARPAT 125:339157 The invention involves a method for treating hyperproliferative conditions (no data ) in mammalian epithelial cells, comprising administering a lysophosphatidic acid deriv. (prepn. given) RC(:X)XCH2CH2CH2YPO3H2 or its cyclic deriv. [Y = 0 or CH2; Z = H, XH or halo; X = 0 or S; R =  $\frac{1}{2}$ (un) substituted (un) satd., straight or branched C11-23 alkyl]. 1-Oleoylglycerol-3-phosphate is an example. The compns. are usable for the treatment of skin cancer, psoriasis, dandruff, etc. lysophosphatidic acid prepn skin hyperproliferative conditions ST IT Skin, disease (lysophosphatidic acids for treating skin hyperproliferative conditions) Lysophosphatidic acids ΙT RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. as agent for treating skin hyperproliferative conditions) 1660-95-3P, Tetraisopropyl methylenediphosphonate 5736-03-8P IT 146508-57-8P 146491-10-3P 147628-64-6P 146491-07-8P 146491-08-9P 158271-50-2P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (intermediate in prepn. of lysophosphatidic acid deriv. for treating skin hyperproliferative conditions) IT 146565-97-1P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. as agent for treating skin hyperproliferative conditions)

146491-11-4P 158271-52-4P 168217-08-1P 65528-98-5P RL: SPN (Synthetic preparation); THU (Therapeutic use) ; BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. as agent for treating skin hyperproliferative conditions) 1623-08-1, Dibenzyl phosphate 4161-56-2, 3-Bromo-2-fluoro-1-propanol IT 24909-72-6, Oleic anhydride 32899-41-5 50651-75-7, Silver 22323-82-6 Dibenzyl phosphate 60134-06-7 RL: RCT (Reactant); RACT (Reactant or reagent) (reactant in prepn. of lysophosphatidic acid deriv. for treating skin hyperproliferative conditions) 146565-97-1P ITRL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. as agent for treating skin hyperproliferative conditions) 146565-97-1 HCAPLUS RN

Hexadecanoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-

Absolute stereochemistry.

CN

yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

- L24 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2003 ACS AN 1995:1006821 HCAPLUS
- DN 124:76506
- TI Preparation of 1-O-acylglycerol-2,3-phosphates and DNA polymerase .alpha. inhibitors containing them
- IN Kobayashi, Susumu; Imai, Nobuyuki; Onimura, Kenjiro; Shinagawa, Rumi; Nakamura, Shuko; Murofushi, Kimiko
- PA Sagami Chem Res, Japan
- SO Jpn. Kokai Tokkyo Koho, 6 pp.

```
CODEN: JKXXAF
DT
    Patent
LA
     Japanese
    ICM C07F009-09
ICS A61K031-665
IC
     1-6 (Pharmacology)
     Section cross-reference(s): 7
FAN.CNT 1
     PATENT NO. KIND DATE
                                          APPLICATION NO. DATE
                                          _____
     JP 07258278 A2 19951009
                                          JP 1994-72837 19940318
PΙ
PRAI JP 1994-72837
                           19940318
    MARPAT 124:76506
GI
CH2OCOR1
CH2-O OM
     The title compds. I (R1 = C10-30 \text{ linear or branched alkenyl, alkynyl; } M =
AB
     H, counter cation) and DNA polymerase .alpha. inhibitors contg. I as
     active ingredients are claimed. The inhibitors are useful as antitumor
     agents. Activities of DNA polymerase .alpha. to produce DNA from
     deoxyribonucleotide triphosphate were 82 and 11% in the presence of I
     [COR1 = (Z)-hexadecenoyl, M = Na] (prepn. given) at 5 or 40 .mu.g/mL,
     resp.
     DNA polymerase inhibitor acylqlycerol phosphate; neoplasm inhibitor
ST
     acylglycerol phosphate
IT
     Neoplasm inhibitors
        (DNA polymerase .alpha. inhibitors contg. 1-0-acylglycerol-2,3-
        phosphates as antitumor agents)
     172360-60-0P 172489-74-6P
TΨ
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (DNA polymerase .alpha. inhibitors contg. 1-0-acylglycerol-2,3-
        phosphates as antitumor agents)
     373-49-9, (Z)-9-Hexadecenoic acid
                                        89155-39-5, 9-Hexadecynoic acid
IT
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (O-acylation of isopropylideneglycerol; DNA polymerase .alpha.
        inhibitors contq. 1-O-acylqlycerol-2,3-phosphates as antitumor agents)
     100-79-8, 2,3-O-Isopropylideneglycerol
IT
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (O-acylation of; DNA polymerase .alpha. inhibitors contg.
        1-O-acylglycerol-2,3-phosphates as antitumor agents)
     37515-61-0P 172360-57-5P 172360-58-6P 172360-59-7P
ΙT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (deprotection of; DNA polymerase .alpha. inhibitors contg.
        1-O-acylglycerol-2,3-phosphates as antitumor agents)
     288-88-0, 1H-1,2,4-Triazole
IT
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction with POCl.beta.; DNA polymerase .alpha. inhibitors contg.
```

1-O-acylglycerol-2,3-phosphates as antitumor agents)

IT 10025-87-3, Phosphoryl chloride

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction with triazole; DNA polymerase .alpha. inhibitors contg.

1-O-acylglycerol-2, 3-phosphates as antitumor agents)

IT 9012-90-2, DNA polymerase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(.alpha.; DNA polymerase .alpha. inhibitors contg. 1-O-acylglycerol-2,3-phosphates as antitumor agents)

IT 172360-60-0P 172489-74-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(DNA polymerase .alpha. inhibitors contg. 1-0-acylglycerol-2,3-phosphates as antitumor agents)

RN 172360-60-0 HCAPLUS

CN 9-Hexadecynoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt (9CI) (CA INDEX NAME)

## Na

RN 172489-74-6 HCAPLUS

CN 9-Hexadecenoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

#### ● Ma

L24 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 1995:638236 HCAPLUS

DN 123:144502

TI Method for preparation of 1-O-acylglycerol 2,3-cyclic phosphate

IN Kobayashi, Susumu; Imai, Nobuyuki; Shinagawa, Rumi; Takahashi, Hideyori

PA Sagami Chem Res, Japan

SO Jpn. Kokai Tokkyo Koho, 31 pp.

CODEN: JKXXAF DTPatent LA Japanese IC ICM C07F009-09 ICS C07F009-6574 ICA A61K031-665; A61K037-22 33-6 (Carbohydrates) Section cross-reference(s): 1, 7 FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE \_\_\_\_ \_\_\_\_\_\_ 19930205 A2 19940816 JP 1993-40657 JP 06228169 PRAI JP 1993-40657 19930205 CASREACT 123:144502; MARPAT 123:144502 GΙ

The title compd. [I; R = linear or branched C1-30 alkyl or C2-30 alkenyl optionally contg. a cycloalkane or an arom. ring; M = H, alkali or alk. earth metal, (un)substituted ammonium] is prepd. by reacting 1-O-acylglycerol RCO2CH2CH(OH)CH2OH (R = same as above) with a phosphorylating agent X1X2X3P(O) [X1 = halo, imidazolyl, triazolyl; X2 = halo, imidazolyl, triazolyl, (un)substituted PhO or alkoxy; X3 = imidazolyl, triazolyl, (un)substituted PhO or alkoxy, substituted amino] followed by hydrolysis. An optically active intermediate (II; m, n = 0-15 integer; R1, R2 = H, HO-protective group) is also prepd. This process gives, in particular, lysophosphatidic acid PHYLPA I (R = Q, M = Na) which is a potent DNA polymerase .alpha. inhibitor and potentially useful as an antitumor agent (no data). Thus, 1-O-[(9S,10R)-9,10-methanohexadecanoyl]-sn-glycerol (prepn. given) in THF was added to a soln. of phosphoryl tristriazolide in THF which was prepd. by reacting triazole with POC13 and Et3N in THF, and the resulting mixt. was stirred at room temp. for 20 min, added to 2% aq. HCl, and extd. with Et2O. The ether ext. was dried over

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anhyd. Na2SO4, treated with NaH in Et2O, and extd. with distd. water
     followed by freeze-drying the water ext. to give 97% optically active
     title compd. (III).
ST
     acylglycerol cyclic phosphate prepn antitumor; DNA polymerase alpha
     inhibitor PHYLPA
ΙT
     Neoplasm inhibitors
        (prepn. of O-acylglycerol cyclic phosphate as DNA polymerase inhibitors
        and antitumor agents)
ΙT
     14347-78-5P, 2,3-O-Isopropylidene-sn-glycerol
                                                     18172-01-5P,
                                    151707-28-7P
     3-Oxabicyclo[3.1.0]hexan-2-ol
                                                    151707-29-8P
                                                                    151707-30-1P
                    151766-40-4P
     151707-31-2P
                                   151766-41-5P
                                                  151766-42-6P
                                                                 151766-43-7P
                    151766-45-9P
                                   151766-46-0P
                                                  151766-48-2P
                                                                  151766-49-3P
     151766-44-8P
     151766-50-6P
                    164215-55-8P
                                   164215-57-0P
                                                  164323-39-1P
                                                                 164323-40-4P
     164323-41-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (intermediate for prepn. of O-acylqlycerol cyclic phosphate as DNA
        polymerase inhibitor)
TΤ
     72741-18-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (phosphorylating agent as intermediate for prepn. of O-acylglycerol
        cyclic phosphate as DNA polymerase inhibitor)
     538-37-4, Dibenzyl phosphorochloridate
                                             777-52-6, p-Nitrophenyl
TΨ
     dichlorophosphate
                         793-10-2, 4-Nitrophenyl phenyl phosphorochloridate
     2524-64-3, Diphenyl phosphorochloridate
                                              16062-77-4
                                                            17672-53-6,
     Bis (2, 2, 2-trichloroethyl) phosphorochloridate
                                                     17677-92-8,
     Bis(2,2,2-trichloro-1,1-dimethylethyl) phosphorochloridate
                                                                   23561-36-6,
                                                      51766-21-3, Phenyl
     2-Chloromethyl-p-nitrophenyl dichlorophosphate
     N-phenylphosphoramidochloridate
                                       57188-46-2, Bis(p-nitrobenzyl)
                           59346-65-5, Di-tert-butyl phosphorobromidate
     phosphorochloridate
     85363-77-5, Bis[2-(p-nitrophenyl)ethyl] phosphorochloridate
                                                                  164215-58-1,
     2-(N, N-Dimethylamino)-4-nitrophenyl phosphorochloridate
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (phosphorylating agent for prepn. of O-acylglycerol cyclic phosphate as
        DNA polymerase inhibitor)
TΤ
     151766-47-1P 151766-51-7P 151766-52-8P
     151766-53-9P 164215-56-9P
     RL: SPN (Synthetic preparation); THU (Therapeutic use)
     ; BIOL (Biological study); PREP (Preparation); USES (Uses)
        (prepn. of O-acylglycerol cyclic phosphate as DNA polymerase inhibitor
        and antitumor agent)
                               14347-83-2, 1-O-Benzyl-2, 3-O-isopropylidene-sn-
IΤ
     334-88-3, Diazo methane
               16495-03-7
                            19670-51-0, (.+-.)-1-0-Hexadecanoylglycerol
     glycerol
     21406-61-1, Pentyltriphenylphosphonium bromide
                                                     22323-82-6
                                                                    50889-30-0,
     (6-Carboxyhexyl) triphenylphosphonium bromide
                                                    89395-28-8
                                                                 115268-48-9.
     (.+-.)-1-O-Hexadecanoyl-2,3-O-isopropylideneglycerol
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction in prepn. of O-acylglycerol cyclic phosphate as DNA
        polymerase inhibitor)
IT
     9012-90-2, DNA polymerase
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (.alpha.; prepn. of O-acylglycerol cyclic phosphate as DNA polymerase
        inhibitors)
TТ
     151766-47-1P 151766-51-7P 151766-52-8P
     151766-53-9P 164215-56-9P
     RL: SPN (Synthetic preparation); THU (Therapeutic use)
     ; BIOL (Biological study); PREP (Preparation); USES (Uses)
        (prepn. of O-acylglycerol cyclic phosphate as DNA polymerase inhibitor
```

and antitumor agent)

RN 151766-47-1 HCAPLUS

CN Cyclopropaneoctanoic acid, 2-hexyl-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (1S,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Na

RN 151766-51-7 HCAPLUS

CN Cyclopropaneoctanoic acid, 2-hexyl-, [(4S)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (1S,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Na

RN 151766-52-8 HCAPLUS

CN Cyclopropaneoctanoic acid, 2-hexyl-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

RN 151766-53-9 HCAPLUS

CN Cyclopropaneoctanoic acid, 2-hexyl-, [(4S)-2-hydroxy-2-oxido-1,3,2-

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

dioxaphospholan-4-yl]methyl ester, sodium salt, (1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

RN 164215-56-9 HCAPLUS

CN Hexadecanoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt (9CI) (CA INDEX NAME)

Na

L24 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 1995:285626 HCAPLUS

DN 122:75127

TI Phospholipids containing two different unsaturated fatty acids for use in therapy, nutrition, and cosmetics

IN Horrobin, David; McMordie, Austin; Manku, Mehar Singh

PA Scotia Holdings PLC, UK

SO Eur. Pat. Appl., 19 pp. CODEN: EPXXDW

DT Patent

LA English

IC ICM C07F009-10

ICS A61K031-66; A61K007-00; A23J007-00; C07F009-117

CC 6-5 (General Biochemistry)

Section cross-reference(s): 1, 17, 62

FAN.CNT 1

LWIN.	-IN T	Τ.															
	PAI	ENT	NO.		KIN	ID DAT	Ξ		AP	PLICA	NOITA	NO.	DATE				
ΡI	ΕP	6090	78		Al	. 199	40803		EP	1994	1-300	599	1994	0127			
		R:	AT,	BE,	CH,	DE, DK	, ES,	FR,	GB, G	GR, ]	E, I	T, LI,	LU,	MC,	NL,	PT,	SE
	CA	2114	349		AΑ	199	40728		CA	1994	-211	4349	1994	0127			
	ИО	9400	288		Α	199	40728		NO	1994	-288		1994	0127			
	ΑU	9454	749		A1	. 199	40804		AU	1994	1-547	49	1994	0127			
	ΑU	6713	29		B2	199	60822										
	ZA	9400	587		Α	199	40909		ZA	1994	1-587		1994	0127			

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JP 06293785
                       Α2
                             19941021
                                            JP 1994-7908
                                                              19940127
     CN 1097124
                        Α
                             19950111
                                            CN 1994-101317
                                                              19940127
                                            US 1994-187042
     US 5466841
                        Α
                             19951114
                                                              19940127
PRAI GB 1993-1629
                             19930127
     A phospholipid comprising two different unsatd. fatty acids, the fatty
     acids being selected from the twelve n-6 and n-3 essential fatty acids,
     oleic acid, parinaric acid and combinic acid are described. The
     phospholipids may be used in prepn. of foods, skin care prepns., or
     pharmaceuticals. The synthesis of phosphatidylcholine contg.
     .gamma.-linolenic acid at the 1 position and oleic acid at the 2 position
     was described.
ST
     phospholipid unsatd fatty acid therapy nutrition; cosmetic phospholipid
     unsatd fatty acid
IT
     Cosmetics
     Food
     Pharmaceuticals
        (phospholipids contq. two different unsatd. fatty acids for use in
        therapy, nutrition, and cosmetics)
IT
     Phosphatidylcholines, biological studies
     Phosphatidylethanolamines
     Phosphatidylinositols
     Phosphatidylserines
     Phospholipids, biological studies
     RL: BUU (Biological use, unclassified); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (phospholipids contq. two different unsatd. fatty acids for use in
        therapy, nutrition, and cosmetics)
IT
     160109-92-2P 160109-97-7P
     RL: BUU (Biological use, unclassified); FFD (Food or feed use); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (phospholipids contq. two different unsatd. fatty acids for use in
        therapy, nutrition, and cosmetics)
ΙT
     506-26-3, .gamma.-Linolenic acid
                                         506-32-1, Arachidonic acid
     Dihomo-.gamma.-linolenic acid
                                      6217-54-5, Docosahexaenoic acid
     10417-94-4, Eicosapentaenoic acid
     RL: BUU (Biological use, unclassified); FFD (Food or feed use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (phospholipids contg. two different unsatd. fatty acids for use in
        therapy, nutrition, and cosmetics)
                                eactions 100-79-8, Solketal 824-94-2, 6609-64-9, 2-Chloro-1,3,2-dioxaphospholane-2-
IT
     75-50-3, Trimethylamine, reactions
     4-Methoxybenzyl chloride
                         64681-08-9, L-.alpha.-Glycerophosphorylcholine
            54562-14-0
     cadmium chloride complex
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (phospholipids contg. two different unsatd. fatty acids for use in
        therapy, nutrition, and cosmetics)
                     160109-93-3P
                                    160109-94-4P
IT
     142924-83-2P
                                                    160109-95-5P
     160109-96-6P
                     160224-75-9P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP
     (Preparation); RACT (Reactant or reagent)
        (phospholipids contg. two different unsatd. fatty acids for use in
        therapy, nutrition, and cosmetics)
TT
     160109-97-7P
     RL: BUU (Biological use, unclassified); FFD (Food or feed use); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (phospholipids contg. two different unsatd. fatty acids for use in
        therapy, nutrition, and cosmetics)
     160109-97-7 HCAPLUS
RN
```

6,9,12-Octadecatrienoic acid, 1-[[(2-oxido-1,3,2-dioxaphospholan-2yl)oxy]methyl]-1,2-ethanediyl ester, (all-Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

160109-96-6P IT

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (phospholipids contg. two different unsatd. fatty acids for use in therapy, nutrition, and cosmetics)

160109-96-6 HCAPLUS RN

6,9,12-Octadecatrienoic acid, 3-[(2-oxido-1,3,2-dioxaphospholan-2-yl)oxy]-2-[(1-oxo-9-octadecenyl)oxy]propyl ester, (all-Z)- (9CI) (CA INDEX NAME) CN

Double bond geometry as shown.

PAGE 1-A

Ме

- (CH<sub>2</sub>)<sub>4</sub>

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ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2003 ACS
AN
     1995:255353 HCAPLUS
     122:31708
DN
ΤI
     Dialkyl (dialkoxyphosphinyl) aminoethyl phosphates as antiinflammatory
     agents
IN
     Johnson, Roy A.
PA
     Upjohn Co., USA
SO
     U.S., 10 pp. Cont.-in-part of U.S. Ser. No. 717,428, abandoned.
     CODEN: USXXAM
DT
     Patent
LA
    English
IC
     ICM C07C261-00
NCL
     558158000
     29-7 (Organometallic and Organometalloidal Compounds)
     Section cross-reference(s): 1
FAN.CNT 2
                                         APPLICATION NO. DATE
    PATENT NO.
                   KIND DATE
                                           -----
    US 5347029 A
                           19940913
                                          US 1993-168441
                                                           19931216
    CA 2102303
                     AA
                           19921220
                                          CA 1992-2102303 19920521
    AT 164163
                     E
                           19980415
                                          AT 1992-913025 19920521
PRAI US 1991-717428
                           19910619
OS
    MARPAT 122:31708
    Provided are novel dialkyl (dialkoxyphosphinyl) methyl phosphates
     (R10)2P(O)CH(CH2NR2R3)OP(O)(OR1)2 which are useful as antiinflammatory and
     anti-arthritic agents. The compds. are synthesized from the reaction of
     tetra-Et oxiranylidenebisphosphonate and unsubstituted or alkylamines.
     Representative compd. include 2-(benzylamino)-1-
     (diethoxyphosphinyl)ethylphosphonic acid di-Et ester, 1-
     (diethoxyphosphinyl) -2-[2'-(1',2',3',4'-tetrahydro) naphthylamino] ethylphos
    phonic acid di-Et ester, 2-(3-fluorobenzylamino)-1-
     (diethoxyphosphinyl)ethylphosphonic acid di-Et ester, and
     5,5-dimethyl-2-\{2-\{3-fluorobenzyl\} amino-1-\{(5,5-dimethyl-1,3,2-
     dioxaphosphorinan-2-yl)oxy]ethyl]-1,3,2-dioxaphosphorinane P,2-dioxide.
ST
     dialkoxyphosphinylaminoethyl phosphate; antiinflammatory
     dialkoxyphosphinylaminoethyl phosphate; antiarthritic
    dialkoxyphosphinylaminoethyl phosphate
IT
    Inflammation inhibitors
        (prepn. of dialkyl (dialkoxyphosphinyl) aminoethyl phosphates as
       antiinflammatory and antiarthritic agents)
ΙT
     Inflammation inhibitors
        (antiarthritics, prepn. of dialkyl (dialkoxyphosphinyl) aminoethyl
       phosphates as antiinflammatory and antiarthritic agents)
IT
    146777-74-4P 146777-75-5P
                                                 146777-77-7P
                                 146777-76-6P
                                                                146777-78-8P
    146777-79-9P 146777-80-2P
                                  146777-81-3P
                                                 146777-82-4P
                                                                146777-83-5P
     146777-84-6P 146777-85-7P
                                  146777-86-8P 146777-87-9P
    146777-88-0P 159759-67-8P
```

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of dialkyl (dialkoxyphosphinyl) aminoethyl phosphates as antiinflammatory and antiarthritic agents) 61-54-1, Tryptamine 64-04-0, Phenethylamine 91-00-9. Aminodiphenylmethane 100-46-9, Benzylamine, reactions 100-82-3, 3-Fluorobenzylamine 107-11-9, Allylamine 108-91-8, Cyclohexylamine, 141-43-5, Ethanolamine, reactions reactions 501-53-1, Benzyl 1660-94-2 2954-50-9 chloroformate 3731-52-0, 3-(Aminomethyl)pyridine 3886-69-9, (R)-(+)-1-Phenylethylamine 5036-48-6, 1-(3-Aminopropyl)imidazole 30525-89-4, Paraformaldehyde RL: RCT (Reactant); RACT (Reactant or reagent) (prepn. of dialkyl (dialkoxyphosphinyl) aminoethyl phosphates as antiinflammatory and antiarthritic agents) 37465-31-9P 141828-19-5P 146777-89-1P TΤ 35335-22-9P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of dialkyl (dialkoxyphosphinyl) aminoethyl phosphates as antiinflammatory and antiarthritic agents) ΙT 146777-87-9P 146777-88-0P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of dialkyl (dialkoxyphosphinyl)aminoethyl phosphates as antiinflammatory and antiarthritic agents) RN 146777-87-9 HCAPLUS CN 1,3,2-Dioxaphosphorinane-2-ethanamine, .beta.-[(5,5-dimethyl-2-oxido-1,3,2dioxaphosphorinan-2-yl)oxy]-N-[(3-fluorophenyl)methyl]-5,5-dimethyl-, 2-oxide (9CI) (CA INDEX NAME)

RN 146777-88-0 HCAPLUS
1,3,2-Dioxaphosphorinane-2-ethanamine, .beta.-[(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]-5,5-dimethyl-N-(2-phenylethyl)-, 2-oxide (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} CH_2-NH-CH_2-CH_2-Ph \\ \hline \\ O & 0 \\ \hline \\ P-CH-O-P \\ \hline \\ Me \\ \end{array}$$

L24 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2003 ACS

AN 1986:533669 HCAPLUS

DN 105:133669

TI Aminopurine derivatives

PA Beecham Group PLC, UK

SO Jpn. Kokai Tokkyo Koho, 14 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM C07D473-32

ICS C07F009-65 ICA A61K031-52

CC 26-9 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 1

FAN.CNT 3

rAN.		TENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI		61085388	A2	19860430	JP 1985-207693	19850919	
	ΕP	05086792 182024	A2	19931214 19860528	EP 1985-111354	19850909	
		182024 182024	A3 B1	19890308 19910403			
		R: BE, CH,	DE, FR	, GB, IT, LI,	LU, NL, SE		
	DK	8504246	Α	19860321	DK 1985-4246	19850918	
	DK	167019	B1	19930816	*		
	ΑU	8547560	A1	19860327	AU 1985-47560	19850918	
	AU	589371	В2	19891012			
	zA	8507149	A	19860827	ZA 1985-7149	19850918	
	CA	1262899	A1	19891114	CA 1985-491028	19850918	
	ES	547128	A1	19870301	ES 1985-547128	19850919	
	CZ	283721	В6	19980617	CZ 1991-3915	19911219	
	JΡ	06025241	A2	19940201	JP 1993-130044	19930507	
	JР	08026021	B4	19960313			
PRAI	GB	1984-23833	A	19840920			
	GB	1985-10331	А	19850423			
		1985-20618	A	19850816			
GI							

```
Title compds. I (R1, R2 = H, acyl, phosphate, etc.) and their salts,
AB
    useful as virucides (no data), were prepd. Thus, refluxing 0.54 g
     2-amino-6-chloro-9-chloro-9-[2-(2,2-dimethyl-1,3-dioxan-3-yl)ethyl]purine
    with 450 mg 10% Pd/C in ethanol and cyclohexane gave 36%
     2-amino-9-[4-hydroxy-3-(hydroxymethyl)-but-1-yl]purine.
ST
     aminopurine ethylpropanediol prepn virucide
    Virucides and Virustats
IT
        (aminopurine derivs.)
IT
     97845-59-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and redn. of)
                    104227-87-4P
     104227-86-3P
                                   104227-88-5P
                                                  104227-89-6P
                                                                 104227-90-9P
TΨ
     104227-91-0P
                    104227-92-1P
                                  104227-93-2P
                                                 104227-94-3P
                                                                 104227-95-4P
     104227-96-5P
                  104227-97-6P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of, as virucide)
ΤТ
     104227-96-5P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of, as virucide)
RN
     104227-96-5 HCAPLUS
     9H-Purin-2-amine, 9-[2-(2-hydroxy-2-oxido-1,3,2-dioxaphosphorinan-5-
CN
     yl)ethyl]- (9CI) (CA INDEX NAME)
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L24 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2003 ACS
     1986:514844 HCAPLUS
ΑN
DN
     105:114844
     Cyclic phosphate esters of substituted 9-(1,3-dihydroxy-2-
ΤI
     propoxymethyl)purines
IN
     Prisbe, Ernest J.; McGee, Daniel P. C.
     Syntex (U.S.A.), Inc., USA
PA
     U.S., 4 pp.
SO
     CODEN: USXXAM
\mathsf{D}\mathbf{T}
     Patent
LA
     English
     ICM C07D473-18
TC
     ICS A61K031-52
     544276000
     26-9 (Biomolecules and Their Synthetic Analogs)
     Section cross-reference(s): 1, 29
FAN.CNT 1
     PATENT NO.
                                             APPLICATION NO. DATE
                       KIND DATE
```

PI US 4590269 A 19860520 US 1984-594508 19840329 PRAI US 1984-594508 19840329 OS CASREACT 105:114844 GI

$$\begin{array}{c|c} Y \\ N \\ N \\ CH_2O \end{array} \begin{array}{c} O \\ P-OZ \\ O \end{array}$$

The title compds. [I; Y = OH, NH2; Z = H, (un)substituted hydrocarbyl, AB cation], useful as antiviral agents (no data), were prepd. Thus, 9-(1,3-dihydro-2-propoxymethyl) guanine in MeCN was reacted with SnCl4 and pyrophosphoryl chloride, followed by workup and chromatog. with NH4OH eluent, to give I (Y = OH, Z = NH4). ST purine cyclic phosphate prepn antiviral Virucides and Virustats TΤ ((dihydroxypropoxymethyl)purine cyclic phosphate esters) IT 13498-14-1 RL: RCT (Reactant); RACT (Reactant or reagent) (phosphorylation by, of (dihydroxypropoxymethyl) guanine) TT 10025-87-3 RL: RCT (Reactant); RACT (Reactant or reagent) (phosphorylation by, of diamino(dihydroxypropoxymethyl)purine) TT 82410-32-0 86629-59-6 RL: RCT (Reactant); RACT (Reactant or reagent) (phosphorylation of) IT 91516-85-7P 91516-89-1P 100683-67-8P 104145-76-8P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of, as antiviral agent) 91516-85-7P 91516-89-1P 100683-67-8P ΙT 104145-76-8P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

RN CN (prepn. of, as antiviral agent)

RN 91516-89-1 HCAPLUS

CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[(2-hydroxy-2-oxido-1,3,2-dioxaphosphorinan-5-yl)oxy]methyl]-, monoammonium salt (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & O & O \\
 & N & N \\
 & N & N \\
 & N & CH_2 - O \\
\end{array}$$

## ● инз

RN 100683-67-8 HCAPLUS

CN 9H-Purine-2,6-diamine, 9-[[(2-hydroxy-2-oxido-1,3,2-dioxaphosphorinan-5-yl)oxy]methyl]- (9CI) (CA INDEX NAME)

RN 104145-76-8 HCAPLUS

CN 9H-Purine-2,6-diamine, 9-[[(2-hydroxy-2-oxido-1,3,2-dioxaphosphorinan-5-yl)oxy]methyl]-, monoammonium salt (9CI) (CA INDEX NAME)

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ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2003 ACS
    1986:207063 HCAPLUS
    104:207063
    N-Alkylquanine acyclonucleosides as antiviral agents
TΙ
IN
    Maccoss, Malcolm; Tolman, Richard L.; Strelitz, Robert A.
PA
    Merck and Co., Inc. , USA
SO
    Eur. Pat. Appl., 29 pp.
    CODEN: EPXXDW
DT
    Patent
LA
    English
    ICM C07D473-18
ICS C07F009-65; A61K031-52; A61K031-675
IC
    26-9 (Biomolecules and Their Synthetic Analogs)
    Section cross-reference(s): 1, 63
FAN.CNT 1
    PATENT NO.
                     KIND DATE
                                          APPLICATION NO. DATE
    EP 161955 A1 19851121
PΙ
                                         EP 1985-400613 19850328
        R: CH, DE, FR, GB, IT, LI, NL
    US 4579849 A 19860401
                                          US 1984-597785
                                                           19840406
    JP 60228480
                      A2
                           19851113
                                         JP 1985-71333
                                                           19850405
PRAI US 1984-597785
                           19840406
    CASREACT 104:207063
GI
```

AB The title compds. I [R1,R2 = C1-19 (halo)alkyl, -alkenyl, -alkynyl or R2 = H; R3 = H, C1-6 alkyl, -hydroxyalkyl; R4 = H, halo, C1-4 alkyl, NH2; R5, R6, R7 = H, OH, C1-6 alkyl, C1-8 acyloxy, C1-6 alkoxy, PO3-, or 2 of R5, R6 = R7 = (-OPO2O-)-, etc.; Z = O, S, CH2; X = anion] useful as antiviral agents (no data) were prepd. Thus, to (S)-9-(2,3-dihydroxy-1-propoxymethyl)guanine in DMSO was added K2CO3 followed by MeI to give (S)-I (R1, R2 = Me; R3, R4 = H; R5, R6 = OH; R7 = Me; X = I) (II). A water-sol. ointment contained II 0.5, glycerol 15, Macrogol 300 20, and PEG 1500 64.5 g.

ST alkylguanine acyclonucleoside prepn antiviral pharmaceutical; guaninium acyclonucleoside prepn antiviral; antiherpetic acyclonucleoside guaninium; quaternization guanine acyclonucleoside; virucide guanine acyclonucleoside prepn

IT Quaternization

(of guanine acyclonucleosides)

IT Virucides and Virustats

(N-alkylguanine acyclonucleosides)

IT Nucleosides, preparation

RL: SPN (Synthetic preparation); PREP (Preparation) (acyclo-, N-alkyl, prepn. of, as antiviral agents)

IT 75-03-6 107-08-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(alkylation by, of (dihydroxypropoxymethyl)guanine)

IT 82410-32-0

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Sackey 09/937386 Page 171
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RL: RCT (Reactant); RACT (Reactant or reagent)
        (alkylation of)
                   102052-83-5
IT
     102052-81-3
                                  102052-85-7
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (as antiviral agent)
IΤ
     111-64-8
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (esterification of, with methyl(dihydroxypropoxymethyl)guanine)
IT
     59277-89-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (methylation of)
IT
     102052-68-6P
                    102052-86-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and quaternization of)
IT
     82145-52-6P
                  102052-67-5P 102052-69-7P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of)
TΤ
     102052-70-0P
                    102052-71-1P
                                   102052-72-2P
                                                   102052-73-3P
                                                                   102052-74-4P
                    102052-76-6P 102052-77-7P 102052-79-9P
     102052-75-5P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of, as antiviral agent)
TΤ
     96480-03-4
                  102052-78-8
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (quaternization of)
TT
     102052-77-7P 102052-79-9P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
  (prepn. of, as antiviral agent)
     102052-77-7 HCAPLUS
RN
     1H-Purinium, 2-amino-6,9-dihydro-9-[[(2-hydroxy-2-oxido-1,3,2-
CN
     dioxaphosphorinan-5-yl)oxy]methyl]-7-methyl-6-oxo-, inner salt (9CI) (CA
     INDEX NAME)
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*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 102052-79-9 HCAPLUS
```

CN 1H-Purinium, 2-amino-6,9-dihydro-9-[[(2-hydroxy-2-oxido-1,3,2-dioxaphosphorinan-5-yl)oxy]methyl]-1,7-dimethyl-6-oxo-, inner salt (9CI) (CA INDEX NAME)

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\*\*\* FRAGMENT DIAGRAM IS INCOMPLETE \*\*\*

07

REP G1=(0-3) C NODE ATTRIBUTES: CONNECT IS E1 RC AT 8 DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS

STEREO ATTRIBUTES: NONE
L5 2167 SEA FILE=REGISTRY SSS FUL L3
L16 STR

CH2-C~O @16 17 18

9 G2 1 G1 3 CH CH2 | 0 8 | 6 0 \$ 0 4 | 6 0 7

CH2·O~~C~~O @12 13 14 15

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Sackey 09/937386 Page 173
REP G1 = (0-3) C
VAR G2=H/AK/10/12/16
NODE ATTRIBUTES:
                        8
CONNECT IS E1 RC AT
CONNECT IS E1 RC AT
                      15
CONNECT IS E1 RC AT
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 18
STEREO ATTRIBUTES: NONE
           2139 SEA FILE=REGISTRY SUB=L5 SSS FUL L16
L19
           1246 SEA FILE=HCAPLUS ABB=ON L18
             30 SEA FILE=HCAPLUS ABB=ON L19(L)THU/RL
L20
L21
            715 SEA FILE=HCAPLUS ABB=ON L19(L) (PREP OR SPN OR IMF)/RL
             21 SEA FILE=HCAPLUS ABB=ON L20 AND L21
L24
           1450 SEA FILE=REGISTRY ABB=ON L18 AND 1-2/NR
L26
           1008 SEA FILE=HCAPLUS ABB≈ON L26
L27
             18 SEA FILE=HCAPLUS ABB=ON L27(L)THU/RL
1,28
L29
              5 SEA FILE=HCAPLUS ABB=ON (L24 OR L28) NOT L24
=> d 129 all 1-5 hitstr
     ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2003 ACS
AN
     2002:905886 HCAPLUS
     137:379994
DN
     Cancerous metastasis inhibitors containing carbacyclic phosphatidic acid
TT
     derivatives
     Mukai, Mutsuko; Kobayashi, Susumu; Murofushi, Hiromu; Murofushi, Kimiko
IN
     Gencom Corporation, Japan
     PCT Int. Appl., 58 pp.
     CODEN: PIXXD2
DΤ
     Patent
     Japanese
LΑ
     ICM A61K031-662
IC
     ICS A61P035-04; C07F009-6574
     1-6 (Pharmacology)
     Section cross-reference(s): 28
FAN.CNT 1
                      KIND DATE
                                             APPLICATION NO. DATE
     PATENT NO.
                                          _____
                     ____
     _____
                       A1
                             20021128
                                            WO 2002-JP4839 20020520
     WO 2002094286
PI
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
              UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI JP 2001-150685
                             20010521
     MARPAT 137:379994
OS
GI
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AB The invention aims at providing novel cancerous metastasis inhibitors by examg. carbacyclic phosphatidic acid derivs. for inhibitory activity against the infiltration of cancer cells. The invention provides cancerous metastasis inhibitors contg. as the active ingredient compds. represented by the general formula I (R is linear or branched C1-30 alkyl, linear or branched C2-30 alkenyl, or linear or branched C2-30 alkynyl, with the proviso that each group may contain a cycloalkane ring or an arom. ring; and M is hydrogen or a counter cation).

ST cancerous metastasis inhibitor carbacyclic phosphatidate deriv antimelanoma

IT Melanoma

(B16; cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT Animal cell line

(HT-1080, infiltration; cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT Human

(cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT Lysophosphatidic acids

RL: BSU (Biological study, unclassified); BIOL (Biological study) (cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT Lung, neoplasm

(metastasis, from melanoma; cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT Antitumor agents

Neoplasm

(metastasis; cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT 60-92-4, CAMP

RL: BSU (Biological study, unclassified); BIOL (Biological study) (cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT 476310-13-1P 476310-14-2P 476310-15-3P

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT 164215-56-9 172360-60-0 476310-07-3

476310-08-4 476310-09-5 476310-10-8

476310-11-9 476310-12-0

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity);

THU (Therapeutic use); BIOL (Biological study); USES (Uses) (cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT 2930-05-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

IT 476310-16-4P 476310-17-5P 476310-18-6P 476310-19-7P 476310-20-0P 476310-21-1P 476310-22-2P 476310-23-3P 476310-24-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Bestmann, H; Chemical Ber 1992, V0.125(1), P225 HCAPLUS
- (2) Sagami Chemical Research Center; JP 06-228169 A 1994 HCAPLUS
- (3) Sagami Chemical Research Center; JP 09-25235 A 1997 HCAPLUS
- (4) Yeda Research And Development Co Ltd; WO 0057864 A 2000 HCAPLUS
- (5) Yeda Research And Development Co Ltd; EP 1162979 A 2000 HCAPLUS
- (6) Yeda Research And Development Co Ltd; AU 3451600 A 2000
- (7) Yokomatsu, T; Heterocycles 1997, V46, P463 HCAPLUS
- 164215-56-9 172360-60-0 476310-07-3 476310-08-4 476310-09-5 476310-10-8

476310-11-9 476310-12-0

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity);

THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cancerous metastasis inhibitors contg. carbacyclic phosphatidic acid derivs.)

- RN 164215-56-9 HCAPLUS
- CN Hexadecanoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt (9CI) (CA INDEX NAME)

#### Na

RN 172360-60-0 HCAPLUS

CN 9-Hexadecynoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt (9CI) (CA INDEX NAME)

Na

RN 476310-07-3 HCAPLUS

CN 5,8,11,14,17-Eicosapentaenoic acid, (2-hydroxy-2-oxido-1,3,2-

KATHLEEN FULLER EIC 1700/PARKER LAW 308-4290

dioxaphospholan-4-yl)methyl ester, sodium salt (9CI) (CA INDEX NAME)

PAGE 1-A

N:

PAGE 1-B

$$=$$
 CH $-$  CH $_2-$  CH $=$  CH $-$  CH $_2-$  CH $=$  CH $-$  Et

RN 476310-08-4 HCAPLUS CN 4,7,10,13,16,19-Docosahexaenoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, sodium salt (9CI) (CA INDEX NAME)

PAGE 1-A

$$\begin{array}{c} O \\ O \\ O \\ O \\ O \\ \end{array} \\ \begin{array}{c} CH_2 - O - C - CH_2 - CH_2 - CH \\ \end{array} \\ \begin{array}{c} CH - CH_2 - CH \\$$

● Na

PAGE 1-B

$$= \mathtt{CH-CH_2-CH} = \mathtt{CH-CH_2-CH} = \mathtt{CH-CH_2-CH} = \mathtt{CH-Et}$$

RN 476310-09-5 HCAPLUS
CN 1,3,2-Dioxaphospholane, 4-[[[8-[(1R,2S)-2-hexylcyclopropyl]octyl]oxy]methy
l]-2-hydroxy-, 2-oxide, sodium salt, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Na

RN 476310-10-8 HCAPLUS

CN 1,3,2-Dioxaphospholane, 4-[(hexadecyloxy)methyl]-2-hydroxy-, 2-oxide, sodium salt (9CI) (CA INDEX NAME)

Na

RN 476310-11-9 HCAPLUS

CN Carbamic acid, [7-[(1R,2S)-2-hexylcyclopropyl]heptyl]-, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, monosodium salt, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Na

RN 476310-12-0 HCAPLUS

CN Carbamic acid, pentadecyl-, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl ester, monosodium salt (9CI) (CA INDEX NAME)

$$^{O}_{HO}$$
  $^{O}_{O}$   $^{O}_{CH_{2}-O-C-NH-(CH_{2})_{14}-Me}$ 

Na

L29 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:834204 HCAPLUS

DN 136:145102

TI Neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells

AU Haimovitz, Rachel; Shinitzky, Meir

CS Department of Biological Chemistry, The Weizmann Institute of Science, Rehovot, 76100, Israel

SO Life Sciences (2001), 69(23), 2711-2723 CODEN: LIFSAK; ISSN: 0024-3205

PB Elsevier Science Inc.

DT Journal

LA English

CC 1-11 (Pharmacology)

AB A series of cyclic glycerophosphates and their deoxy analogs were tested for induction of neuronal outgrowth in PC12 cells. Under chronic presence of a cyclic phosphate PC12 cells developed distinct isles of neuronal networks which covered up to 20% of the culture area, while .alpha. and .beta. glycerophosphates (the neg. control compds.) did not induce any neuronal outgrowth. Distinct isles of neuronal networks were also obsd. upon short term application (i.e. 2 pulses of 3 h each at day 1 and day 4) of the tested cyclic phosphates in contrast to an analogous short term exposure to NGF which was abortive. Anal. of tyrosine phosphorylation indicated a battery of phosphorylated proteins after several minutes of application of the cyclic phosphates, among which was an ERK protein of .apprx.63kD (possibly ERK7). Nerve rescue expts. were carried out with NGF differentiated PC12 cells where NGF was replaced with either 1,2 or 1,3 cyclic propanediolphosphate (1,2 cPP and 1,3 cPP) for 7 days. A distinct dose dependent preservation of neuronal network by these compds. was obsd. In the control cultures NGF deprivation resulted in massive neuronal retraction and cell death. Preliminary expts. indicated that the nerve rescue by the cyclic phosphates involves the increase in the level of CASPase 6. The above findings suggest that cyclic glycerophosphates and their analogs may bear important physiol. and pharmacol. implications which are currently under investigation.

ST neuron differentiation cyclic phosphate nerve regeneration

IT Nerve

(differentiation; neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells)

IT Regeneration, animal

(nerve; neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells)

IT Neurotrophic factors

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells)

- Sackey 09/937386 Page 179 Cell differentiation (neuronal; neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells) Phosphorylation, biological IT (protein tyrosine; neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells) IT (regeneration; neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells) ΙT Phosphoproteins RL: BSU (Biological study, unclassified); BIOL (Biological study) (tyrosine-contg., phosphorylation; neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells) 182372-15-2, CASPase 6 222838-93-9, Protein kinase ERK7 ΙT RL: BSU (Biological study, unclassified); BIOL (Biological study) (neuronal outgrowth and rescue induced by cyclic phosphates in PC12 362-74-3, Dibutyryl ΙT 57-03-4, .alpha.-Glycerophosphate 60-92-4, CAMP CAMP 711-07-9 13507-10-3 17181-54-3, .beta.-Glycerophosphate 20636-79-7 25664-08-8 42320-97-8 286020-33-5 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells) THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 28 (1) Abe, N; Molecular Cell Biololgy 1999, V19, P1301 (2) Berridge, M; Annual Review of Biochemistry 1987, V56, P159 HCAPLUS (3) Boulton, T; Cell 1991, V65, P663 HCAPLUS (4) Bredesen, D; Annals of Neurology 1995, V38, P839 MEDLINE (5) Cowley, S; Cell 1994, V77, P841 HCAPLUS (6) Dawson, R; Biochemical Journal 1971, V122, P605 HCAPLUS (7) Frodin, M; Journal of Biological Chemistry 1994, V269, P6207 HCAPLUS (8) Ginty, D; Cell 1994, V77, P713 (9) Glowacka, D; Journal of Neuroscience Research 1990, V25, P453 HCAPLUS (10) Greene, L; Advances in Cellular Neurobiology 1982, V3, P373 HCAPLUS (11) Greene, L; Journal of Cell Biology 1978, V78, P747 HCAPLUS (12) Greene, L; Proceedings of the National Academy of Sciences USA 1976, V73, P2424 HCAPLUS (13) Gunning, P; Journal of Cell Biology 1981, V89, P240 HCAPLUS (14) Gunning, P; Journal of Neuroscience 1981, V1, P1085 HCAPLUS (15) Heidemann, S; Journal of Cell Biology 1985, V100, P916 HCAPLUS (16) Huang, C; Journal of Neurochemistry 1996, V67, P530 HCAPLUS (17) Kaplan, D; Nature 1991, V350, P158 HCAPLUS (18) Martin, D; Journal of Neurobiology 1992, V23, P1205 HCAPLUS
- (19) Ohimichi, M; Journal of Biological Chemistry 1992, V267, P21601
- (20) Ohimichi, M; Journal of Biological Chemistry 1994, V269, P1143
- (21) Richter-Landsberg, C; Journal Cell Biology 1986, V102, P821 HCAPLUS
- (22) Ross, T; Journal of Biological Chemistry 1986, V261, P11119 HCAPLUS
- (23) Rouser, G; Biological Membranes 1968, P5 HCAPLUS
- (24) Rydel, R; Proceedings of the National Academy of Sciences USA 1998, V85, P1257
- (25) Shinitzky, M; European Journal of Biochemistry 2000, V267, P2547 HCAPLUS
- (26) Shinitzky, M; Journal of Biological Chemistry 1993, V268, P14109 HCAPLUS
- (27) Young, S; FEBS Letters 1994, V338, P212 HCAPLUS (28) Yung, Y; FEBS Letters 1997, V408, P292 HCAPLUS
- 711-07-9 13507-10-3 20636-79-7 25664-08-8 42320-97-8 286020-33-5
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(neuronal outgrowth and rescue induced by cyclic phosphates in PC12 cells)

RN 711-07-9 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 13507-10-3 HCAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 20636-79-7 HCAPLUS

CN 1,3,2-Dioxaphospholane, 2-hydroxy-4-methyl-, 2-oxide (9CI) (CA INDEX NAME)

RN 25664-08-8 HCAPLUS

CN 1,3,2-Dioxaphospholane-4-methanol, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 42320-97-8 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 286020-33-5 HCAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

L29 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:402490 HCAPLUS

DN 131:208765

TI Inhibition of tumor invasion and metastasis by a novel lysophosphatidic acid (cyclic LPA)

AU Mukai, Mutsuko; Imamura, Fumio; Ayaki, Masako; Shinkai, Kiyoko; Iwasaki, Teruo; Murakami-Murofushi, Kimiko; Murofushi, Hiromu; Kobayashi, Susumu; Yamamoto, Takashi; Nakamura, Hiroyuki; Akedo, Hitoshi

CS Department of Tumor Biochemistry, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan

SO International Journal of Cancer (1999), 81(6), 918-922 CODEN: IJCNAW; ISSN: 0020-7136

PB Wiley-Liss, Inc.

DT Journal

LA English

CC 1-6 (Pharmacology)

Fetal calf serum (FCS) and 1-oleoyl lysophosphatidic acid (LPA) were previously found to be potent inducers of invasion (transcellular migration) in an in vitro system. A novel LPA, composed of cyclic phosphate and cyclopropane-contg. hexadecanoic acid (PHYLPA), first isolated from myxoamoebae of Physarum polycephalum, and its synthetic derivs. (cLPA) were tested for their ability to inhibit tumor cell invasion and metastasis. Among these, Pal-cLPA, which has a palmitoyl moiety, was most potent in inhibiting invasion, with 93.8% inhibition at the concn. of 25 .mu.M. Invasion in vitro by mouse melanoma cells (B16), human pancreatic adenocarcinoma cells (PSN-1), human lung cancer cells (OC-10) and human fibrosarcoma cells (HT-1080) was also inhibited by Pal-cLPA. The stimulation of MMI cells with LPA triggered F-actin formation, which was impaired by the addn. of Pal-cLPA at invasion-inhibitory concn. Pal-cLPA induced a rapid increase in adenosine 3',5'-cyclic monophosphate (cAMP) concn. in MMI cells. The addn. of dibutyryl cAMP significantly abrogated LPA-induced invasion by MMI cells and actin polymn. in the cells. The inhibition of MM I cell invasion by Pal-cLPA may be ascribed to an increased level of cAMP. Pal-cLPA also suppressed invasion in vitro by MMI cells induced by FCS dose dependently, without affecting proliferation. It also suppressed the pulmonary metastasis of B 16 mouse melanoma cells injected into the tail vein of C57BL/6 mice. Thus, Pal-cLPA is effective in inhibiting invasion and

```
metastasis of a variety of tumor cells.
     metastasis antitumor lysophosphatidic acid
ST
TΤ
     Antitumor agents
        (metastasis; inhibition of tumor invasion and metastasis by a novel
        lysophosphatidic acid derivs.)
     151766-47-1 168217-08-1 168217-09-2
IT
     168217-10-5 169736-88-3 188171-56-4
     188171-62-2
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (inhibition of tumor invasion and metastasis by a novel
        lysophosphatidic acid derivs.)
     60-92-4, Adenosine 3',5'-cyclic monophosphate
     RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
     study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (inhibition of tumor invasion and metastasis by a novel
        lysophosphatidic acid derivs.)
RE.CNT
              THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Akedo, H; Cancer Res 1986, V46, P2416 MEDLINE
(2) Akedo, H; Invasion Metastasis 1988, V9, P134
(3) Friedman, P; J biol Chem 1996, V271, P953 HCAPLUS
(4) Gohla, A; J biol Chem 1998, V273, P4653 HCAPLUS
(5) Guo, Z; Proc nat Acad Sci (Wash) 1996, V93, P14367 HCAPLUS
(6) Ha, K; J Cell Biol 1993, V123, P1789 HCAPLUS
(7) Hall, A; Science 1998, V280, P2074 HCAPLUS
(8) Hecht, J; J Cell Biol 1996, V135, P1071 HCAPLUS
(9) Imamura, F; Biochem biophys Res Comm 1993, V193, P497 HCAPLUS
(10) Imamura, F; Int J Cancer 1996, V65, P627 HCAPLUS
(11) Kobayashi, S; Tetrahedron Lett 1993, V34, P4047 HCAPLUS
(12) Lang, P; EMBO J 1996, V15, P510 HCAPLUS
(13) Liliom, K; Amer J Physiol 1996, V270, PC772 HCAPLUS
(14) Moolenaar, W; Curr Opinion Cell Biol 1997, V9, P168 HCAPLUS
(15) Murakami-Murofushi, K; Cell Struct Funct 1993, V18, P363 HCAPLUS
(16) Murakami-Murofushi, K; J biol Chem 1992, V267, P21512 HCAPLUS
(17) Sekine, A; J biol Chem 1989, V264, P8602 HCAPLUS
(18) Stam, J; EMBO J 1998, V17, P4066 HCAPLUS
(19) van Corven, E; Cell 1989, V59, P45 HCAPLUS
(20) Yoshioka, K; J biol Chem 1998, V273, P5146 HCAPLUS
     151766-47-1 168217-08-1 168217-09-2
     168217-10-5 169736-88-3 188171-56-4
     188171-62-2
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (inhibition of tumor invasion and metastasis by a novel
        lysophosphatidic acid derivs.)
RN
     151766-47-1 HCAPLUS
     Cyclopropaneoctanoic acid, 2-hexyl-, [(4R)-2-hydroxy-2-oxido-1,3,2-
CN
     dioxaphospholan-4-yl]methyl ester, sodium salt, (1S,2R)- (9CI) (CA INDEX
```

Absolute stereochemistry. Rotation (+).

NAME)

N a

RN 168217-08-1 HCAPLUS

CN Hexadecanoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

RN 168217-09-2 HCAPLUS

CN 9-Hexadecenoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (9Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

Na

RN 168217-10-5 HCAPLUS

CN 9-Hexadecynoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

RN 169736-88-3 HCAPLUS

CN 9-Octadecenoic acid (9Z)-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HO 
$$\stackrel{\text{O}}{\underset{\text{O}}{\text{R}}}$$
  $\stackrel{\text{O}}{\underset{\text{O}}{\text{O}}}$   $\stackrel{\text{O}}{\underset{\text{CH}_2)}{\text{7}}}$   $\stackrel{\text{Me}}{\underset{\text{CH}_2)}{\text{7}}}$ 

Na

RN 188171-56-4 HCAPLUS

CN 9-Hexadecenoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (9E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

Na

RN 188171-62-2 HCAPLUS

CN Eicosanoic acid, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

#### Na

MARPAT 123:350234

OS GI

```
L29 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS
AN
    1995:951163 HCAPLUS
DN
     Promoters of protein phosphokinase C activation containing
TΙ
     1-O-acylglycerol 2,3-cyclic phosphate
     Kobayashi, Susumu; Imai, Nobuyuki; Onimura, Kenjiro; Nakamura, Shuko;
IN
    Murofushi, Kimiko
     Sagami Chem Res, Japan
PΆ
SO
     Jpn. Kokai Tokkyo Koho, 6 pp.
     CODEN: JKXXAF
DT
     Patent
LA
     Japanese
     ICM C07F009-10
IC
     ICS C07F009-6571; C12N009-00
CC
     63-5 (Pharmaceuticals)
FAN.CNT 1
     PATENT NO.
                      KIND
                            DATE
                                           APPLICATION NO.
     JP 07149772
                       A2
                            19950613
                                           JP 1993-319186
                                                            19931126
PRAI JP 1993-319186
                            19931126
```

AB A promoter for activation of protein phosphokinase C (PKC) contains 1-O-acylglycerol 2,3-cyclic phosphate [I; R = linear or branched C1-30 alkyl or C2-30 alkenyl optionally contg. a cycloalkane or an arom. ring; M = H, alkali or alk. earth metal, (un)substituted NH4] as the active ingredient. It is useful for the treatment of hypertension, hyperglycemia, and dementia. For example, 1-O-[(9S,10R)-9,10-methanohexadecanoyl]-sn-glycerol 2,3-cyclic phosphate sodium salt (II) in vitro promoted 8.1 times the activity of cPKC.alpha. in an assay using [32P]ATP and leupeptin as compared to the control.

ST acylglycerol cyclic phosphate; promoter protein kinase C activation; hypertension treatment acylglycerol cyclic phosphate; hyperglycemia treatment acylglycerol cyclic phosphate; dementia treatment acylglycerol

cyclic phosphate

IT Antidiabetics and Hypoglycemics

Antihypertensives

(promoters of protein phosphokinase C activation contg. acylglycerol cyclic phosphates for treating hypertension, hyperglycemia, and dementia)

IT Mental disorder

(dementia, promoters of protein phosphokinase C activation contg. acylglycerol cyclic phosphates for treating hypertension, hyperglycemia, and dementia)

IT 151766-47-1 151766-51-7 151766-52-8 151766-53-9 170908-55-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(promoters of protein phosphokinase C activation contg. acylglycerol cyclic phosphates for treating hypertension, hyperglycemia, and dementia)

IT 141436-78-4, Protein kinase c

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(promoters of protein phosphokinase C activation contg. acylglycerol cyclic phosphates for treating hypertension, hyperglycemia, and dementia)

IT 151766-47-1 151766-51-7 151766-52-8 151766-53-9 170908-55-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(promoters of protein phosphokinase C activation contg. acylglycerol cyclic phosphates for treating hypertension, hyperglycemia, and dementia)

RN 151766-47-1 HCAPLUS

CN Cyclopropaneoctanoic acid, 2-hexyl-, [(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (1S,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Na

RN 151766-51-7 HCAPLUS

CN Cyclopropaneoctanoic acid, 2-hexyl-, [(4S)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt, (1S,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Na

151766-52-8 HCAPLUS RN

Cyclopropaneoctanoic acid, 2-hexyl-, [(4R)-2-hydroxy-2-oxido-1,3,2-CN dioxaphospholan-4-yl]methyl ester, sodium salt, (1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

151766-53-9 HCAPLUS RN

Cyclopropaneoctanoic acid, 2-hexyl-, [(4S)-2-hydroxy-2-oxido-1,3,2-CN dioxaphospholan-4-yl]methyl ester, sodium salt, (1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

170908-55-1 HCAPLUS RN

Heptadecanoic acid, (2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl)methyl CN ester, sodium salt, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

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L29 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2003 ACS
AN
     1973:52525 HCAPLUS
     78:52525
DN
     Novel phosphate anthelmintics. 1. Alkyl 2,2-dichlorovinyl methyl
ΤI
     phosphates and related alkoxyalkyl and cycloalkyl analogs of dichlorvos
     Morales, Juan G.; Whetstone, Richard H.; Stoutamire, Donald W.; Hass, D.
ΑU
     Biol. Sci. Res. Cent., Shell Dev. Co., Modesto, CA, USA
CS
     Journal of Medicinal Chemistry (1972), 15(12), 1225-31
SO
     CODEN: JMCMAR; ISSN: 0022-2623
\mathsf{DT}
     Journal
     English
LA
     1-3 (Pharmacodynamics)
CC
     Section cross-reference(s): 23
     Alkyl 2,2-dichlorovinyl Me phosphates showed anthelmintic activity which
     increased with increasing chain length (hydrophobicity) to a max. at
     C7-C10. Thus, 2,2-dichlorovinyl n-heptyl Me phosphate (I) [23248-43-3]
     showed an ED50 of 2 mg/kg orally against Syphacia obvelata in mice, with a
     max. tolerated dose of 500 mg/kg, and gave 50% inhibition of fly head cholinesterase [9001-08-5] at 2.5 .tim. 10-10M. N-decyl 2,2-dichlorovinyl
     Me phosphate [23248-45-5] gave max. inhibition of Hymenolepis nana in mice
     (ED50 16 mg/kg orally, max. tolerated dose 500 mg/kg). The C2-C4
     .omega.-chloroalkyl esters and the di-Pr and di-Bu esters had higher
     therapeutic indexes than the asymmetric n-alkyl analogs. To synthesize I,
     dichlorvos was refluxed with KI in Me2CO to form Na 2,2-dichlorovinyl Me
     phosphate, which was converted to the acid with HCl. This acid was
     converted with SOC12 to P,P'-bis(2,2-dichlorovinyl) P,P'-dimethyl
     pyrophosphate, which underwent alcoholysis with n-heptanol to form I.
     dichlorvos analog anthelmintic; phosphate alkyl chlorovinyl anthelmintic
ST
     Molecular structure-biological activity relationship
IT
         (anthelmintic, of dichlorvos analogs)
ΙT
     Anthelmintics
         (dichlorvos analogs)
               71-98-7 72-00-4
                                  2597-51-5
                                                3212-19-9
                                                            3309-70-4
     62-73-7
                 5301-38-2 5301-43-9 5301-54-2
                                                    13445-62-0 17196-86-0
     5266-08-0
                  17196-88-2 17196-89-3
                                             17196-92-8 18795-58-9
     17196-87-1
                                                          23248-42-2
                                23248-40-0
                                             23248-41-1
                  20202-93-1
     20202-81-7
                                23248-45-5
                                             23248-46-6
                                                          25561-01-7
                  23248-44-4
     23248-43-3
                                                          34641-40-2
                 34622-69-0
                                34622-70-3
                                             34622-78-1
     34622-68-9
                                             40282-70-0
                                                          40282-76-6
     35075-19-5
                 40282-65-3
                                40282-68-6
                                                          40282-90-4
                                             40282-88-0
     40282-78-8
                  40282-81-3
                                40282-82-4
                                             40282-98-2
                                                          40282-99-3
                                40282-97-1
                  40282-96-0
     40282-95-9
                                40283-03-2 40283-04-3 40284-62-6
                   40283-02-1
     40283-00-9
     40929-79-1
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
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NEWS 35

NEWS 36

NEWS 37

Dec 17

Dec 17

Dec 17

Dec 30

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TOXCENTER enhanced with additional content

ISMEC no longer available

Adis Clinical Trials Insight now available on STN

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NEWS 40 Jan 21 NUTRACEUT offering one free connect hour in February 2003
NEWS 41 Jan 21 PHARMAML offering one free connect hour in February 2003
NEWS 42 Jan 29 Simultaneous left and right truncation added to COMPENDEX,
ENERGY, INSPEC

NEWS EXPRESS

January 6 CURRENT WINDOWS VERSION IS V6.01a,
CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002

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FILE 'HOME' ENTERED AT 16:48:59 ON 06 FEB 2003

=> file reg COST IN U.S. DOLLARS

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STRUCTURE FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4 DICTIONARY FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties

in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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**** START OF FIELD ****
             0 --> 188171-62-2/PN
E3
                   AU699075/PN
E4
             4
                   AU701954/PN
E5
             4
                   AU709385/PN
E6
             4
E7
             8
                   AU711559/PN
E8
            16
                   AU715462/PN
            24
                   AU717638/PN
E9
            10
                   AU723178/PN
E10
                   AU724493/PN
            12
E11
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E12
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E2
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E3
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E5
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E6
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E7
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188171-67-77RN
188171-68-87RN
188171-69-97RN
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E8
E9
             1
E10
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E11
                   188171-71-3/RN
E12
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=> s e3
              1 188171-62-2/RN
=> file caplus
                                                    SINCE FILE
COST IN U.S. DOLLARS
                                                         ENTRY
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FILE 'CAPLUS' ENTERED AT 16:50:39 ON 06 FEB 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

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TOTAL

SESSION 1.41

1.20

FILE COVERS 1907 - 6 Feb 2003 VOL 138 ISS 6 FILE LAST UPDATED: 5 Feb 2003 (20030205/ED)

FULL ESTIMATED COST

This file contains CAS Registry Numbers for easy and accurate substance identification.

 $\Rightarrow$  s 11

2 L1 L2

=> d 12 ibib abs hitstr 1-2

ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS 1999:402490 CAPLUS ACCESSION NUMBER:

131:208765 DOCUMENT NUMBER:

Inhibition of tumor invasion and metastasis by a TITLE:

novel

lysophosphatidic acid (cyclic LPA)

Mukai, Mutsuko; Imamura, Fumio; Ayaki, Masako; AUTHOR(S):

Shinkai, Kiyoko; Iwasaki, Teruo; Murakami-Murofushi,

Kimiko; Murofushi, Hiromu; Kobayashi, Susumu;

Yamamoto, Takashi; Nakamura, Hiroyuki; Akedo, Hitoshi

Department of Tumor Biochemistry, Osaka Medical CORPORATE SOURCE:

Center

for Cancer and Cardiovascular Diseases, Osaka, Japan

International Journal of Cancer (1999), 81(6),

SOURCE: 918-922

CODEN: IJCNAW; ISSN: 0020-7136

Wiley-Liss, Inc. PUBLISHER:

Journal DOCUMENT TYPE: English LANGUAGE:

Fetal calf serum (FCS) and 1-oleoyl lysophosphatidic acid (LPA) were previously found to be potent inducers of invasion (transcellular migration) in an in vitro system. A novel LPA, composed of cyclic phosphate and cyclopropane-contq. hexadecanoic acid (PHYLPA), first isolated from myxoamoebae of Physarum polycephalum, and its synthetic derivs. (cLPA) were tested for their ability to inhibit tumor cell invasion and metastasis. Among these, Pal-cLPA, which has a palmitoyl moiety, was most potent in inhibiting invasion, with 93.8% inhibition at the concn. of 25 .mu.M. Invasion in vitro by mouse melanoma cells (B16), human pancreatic adenocarcinoma cells (PSN-1), human lung cancer cells (OC-10) and human fibrosarcoma cells (HT-1080) was also inhibited by Pal-cLPA. The stimulation of MMI cells with LPA triggered F-actin formation, which was impaired by the addn. of Pal-cLPA at

invasion-inhibitory concn. Pal-cLPA induced a rapid increase in

adenosine

3',5'-cyclic monophosphate (cAMP) concn. in MMI cells. The addn. of dibutyryl cAMP significantly abrogated LPA-induced invasion by MMI cells and actin polymn. in the cells. The inhibition of MM I cell invasion by Pal-cLPA may be ascribed to an increased level of cAMP. Pal-cLPA also suppressed invasion in vitro by MMI cells induced by FCS dose

dependently,

without affecting proliferation. It also suppressed the pulmonary metastasis of B 16 mouse melanoma cells injected into the tail vein of C57BL/6 mice. Thus, Pal-cLPA is effective in inhibiting invasion and metastasis of a variety of tumor cells.

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)

(inhibition of tumor invasion and metastasis by a novel lysophosphatidic acid derivs.)

188171-62-2 CAPLUS RN

Eicosanoic acid, CN

[(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

REFERENCE COUNT:

THERE ARE 20 CITED REFERENCES AVAILABLE FOR 20

THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS 1997:237764 CAPLUS

ACCESSION NUMBER:

DOCUMENT NUMBER:

126:220705

TITLE:

Tumor metastasis inhibitors containing

1-0-acylqlycerol-2,3-phosphates

INVENTOR(S):

Kobayashi, Susumu; Matsumoto, Myoko; Onimura,

Kenjiro;

Aketo, Hitoshi; Aragai, Kyoko; Mukai, Michiko

PATENT ASSIGNEE(S):

Sagami Chem Res, Japan

SOURCE:

Jpn. Kokai Tokkyo Koho, 11 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09025235	A2	19970128	JP 1995-177170	19950713
PRIORITY APPLN. INFO.	:	JP	1995-177170	19950713
OTHER SOURCE(S):	MA	RPAT 126:220705		

Page 6

Ι

The metastasis inhibitors contain the title compds. I (R = C2-30 linear AΒ or branched alkyl, alkenyl, alkynyl which may contain cycloalkane ring; M =H, counter cation) as active ingredients. I (COR = palmitoyl, M = Na) (prepn. given) at 25 .mu.M showed >99% inhibition against 1-0-oleoyllysophosphatidic acid-induced infiltration of rat ascites hepatoma cell (MM1) into a cultured monolayer of peritoneal mesothelial cells, vs. 96% at 12.5 .mu.M for PHYLPA. 188171-62-2P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of 1-O-acylglycerol-2,3-phosphates as tumor metastasis inhibitors)

RN 188171-62-2 CAPLUS

CN Eicosanoic acid,

[(4R)-2-hydroxy-2-oxido-1,3,2-dioxaphospholan-4-yl]methyl ester, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	9.91	11.32
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ANSWER (12 OF 19 CAPLUS COPYRIGHT 2003 ACS L18

1986:591264 CAPLUS ΑN

105:191264 DN

Structure of two isomeric 1,3,2-dioxaphosphorinanes ΤI

Jones, A. S.; Kumar, A.; Walker, R. T. ΑU

Chem. Dep., Birmingham Univ., Birmingham, B15 2TT, UK CS

Journal of Organic Chemistry (1986), 51(22), 4310-11 SO CODEN: JOCEAH; ISSN: 0022-3263

DTJournal

LΑ English

CASREACT 105:191264 OS

The 2 isomer 5-hydroxy-2-methoxy-1,3,2-dioxaphosphacyclohexane 2-oxide AB were prepd. sep. by stereospecific syntheses, and their structures were confirmed by 13C, 31P and 1H and x-ray crystallog.

ΙT 104532-42-5P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and configuration of, carbon-13 and phosphorus-31 and proton NMR in relation to)

104532-42-5 CAPLUS RN

1,3,2-Dioxaphosphorinan-5-ol, 2-methoxy-, 2-oxide, cis- (9CI) (CA INDEX CN NAME)

Relative stereochemistry.

IT 104532-44-7P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn., crystal structure, and carbon-13, phosphorus-31, and proton

104532-44-7 CAPLUS RN

1,3,2-Dioxaphosphorinan-5-ol, 2-methoxy-, 2-oxide, trans- (9CI) CN INDEX The second secon

NAME)

Relative stereochemistry.

L18 ANSWER 7/OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 1996:465566 CAPLUS

DN 125:221961

TI Synthesis and structure of some stable phospholane-phospholanes

AU Nifantyev, E. E.; Koroteev, A. M.; Koroteev, M. P.; Meshkov, S. V.; Belsky, V. K.; Bekker, A. R.

CS Dep. Chem., V. I. Lenin Moscow State Pedagogical Univ., Moscow, 119021, Russia

SO Phosphorus, Sulfur and Silicon and the Related Elements (1996), 113(1-4), 1-13

CODEN: PSSLEC; ISSN: 1042-6507

PB Gordon & Breach

DT Journal

LA English

GΙ

Bicyclophosphites, e.g., I (R = R' = trityloxymethyl; R = H, R' = 2-Ph-1,2,3-triazolyl-4), based on linear 1,2,3-triols with terminal substituents, i.e., RCH(OH)CH(OH)CH(OH)R' (1), are stable and were prepd. from 1 and P[NMe2]3 in benzene. Thus hitherto unknown phospholane-phospholane esters, namely, I (R = H, R' = Ph, Et), including optically active ones, were synthesized and their promise for synthetic use (via chlorination, H2O2-oxidn. and amination) was demonstrated. The structure of the new compds. was proved by 1H, 13C and 31P NMR spectroscopy and the crystal x-ray anal. of 2-oxo-2,5-dihydroxy-4-phenyl-1,3,2-dioxaphosphorinane II (X = NC5H10) was detd.

IT 181488-10-8P 181656-46-2P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (crystal structure)

RN 181488-10-8 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-4-phenyl-, 2-oxide, (4R-cis)-, compd. with piperidine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 181258-01-5 CMF C9 H11 O5 P

Absolute stereochemistry.

CM 2

CRN 110-89-4 CMF C5 H11 N

RN 181656-46-2 CAPLUS CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-4-phenyl-, 2-oxide, (4S-trans)-, compd. with piperidine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 181488-13-1 CMF C9 H11 O5 P

Absolute stereochemistry.

CM 2

CRN 110-89-4 CMF C5 H11 N

# IT 181258-01-5P 181258-02-6P 181488-13-1P 181488-14-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. and amination reactions of)

Ben

RN 181258-01-5 CAPLUS CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-4-phenyl-, 2-oxide, (4R-cis)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 181258-02-6 CAPLUS
CN 1,3,2-Dioxaphosphorinan-5-ol, 4-ethyl-2-hydroxy-, 2-oxide, (4R-cis)(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

RN 181488-13-1 CAPLUS CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-4-phenyl-, 2-oxide, (4S-trans)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 181488-14-2 CAPLUS CN 1,3,2-Dioxaphosphorinan-5-ol, 4-ethyl-2-hydroxy-, 2-oxide, (4S-trans)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Ben

IT 181488-08-4P 181488-09-5P 181656-45-1P

RN 181488-08-4 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 4-ethyl-2-hydroxy-, 2-oxide, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 181488-07-3 CMF C5 H11 O5 P

CM 2

CRN 75-64-9 CMF C4 H11 N

RN 181488-09-5 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-4-phenyl-, 2-oxide, (4R-cis)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 181258-01-5

Ben

CMF C9 H11 O5 P

Absolute stereochemistry.

CM 2

CRN 75-64-9 CMF C4 H11 N

$$\begin{array}{c} {\rm ^{NH_2}} \\ {\rm ^{H_3C-}\,C-\,CH_3} \\ {\rm ^{CH_3}} \end{array}$$

RN 181656-45-1 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-4-phenyl-, 2-oxide, (4S-trans)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM ]

CRN 181488-13-1 CMF C9 H11 O5 P

Absolute stereochemistry.

CM 2

CRN 75-64-9 CMF C4 H11 N

history

Ben

≈> d his

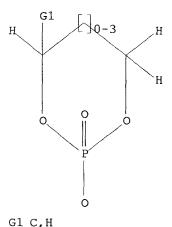
(FILE 'STNGUIDE' ENTERED AT 17:28:12 ON 22 JAN 2003)
DEL HIS Y

FILE 'REGISTRY' ENTERED AT 17:30:12 ON 22 JAN 2003 L1STRUCTURE UPLOADED L250 S L1 70336 S 1-3/NR AND 0-1/P AND 0/N AND 4-10/0 L350 S L1 SAM SUB=L3 L41194 S L1 FUL SUB=L3 L5 FILE 'CAPLUS' ENTERED AT 17:33:47 ON 22 JAN 2003 L6 842 S L5 FILE 'STNGUIDE' ENTERED AT 17:34:19 ON 22 JAN 2003 FILE 'REGISTRY' ENTERED AT 17:34:41 ON 22 JAN 2003 FILE 'STNGUIDE' ENTERED AT 17:35:31 ON 22 JAN 2003 FILE 'REGISTRY' ENTERED AT 17:36:56 ON 22 JAN 2003 L7 STRUCTURE UPLOADED STRUCTURE UPLOADED  $\Gamma8$ L9 STRUCTURE UPLOADED 0 S L7 SAM SUB=L5 L103 S L7 FUL SUB=L5 L1135 S L8 FUL SUB=L5 L12 L13 610 S L9 FUL SUB=L5 648 S L11 OR L12 OR L13 L143941227 S 2-5/NC L15 L16 648 S L14 SUB=L14

FILE 'CAPLUS' ENTERED AT 17:42:23 ON 22 JAN 2003

L17 4 S L11 L18 19 S L12

=> d 11; d 17; d 18; d 19; d 110; d his L1 HAS NO ANSWERS L1 STR



Structure attributes must be viewed using STN Express query preparation.

G1 C,H

Structure attributes must be viewed using STN Express query preparation.

G1 C,H

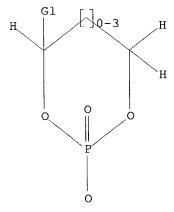
Structure attributes must be viewed using STN Express query preparation.

L9 HAS NO ANSWERS L9 STR

G1 C,H

Structure attributes must be viewed using STN Express query preparation.

L10 HAS NO ANSWERS STR L1



G1 C, H

Structure attributes must be viewed using STN Express query preparation. L3 70336 SEA FILE=REGISTRY ABB=ON PLU=ON 1-3/NR AND 0-1/P AND 0/N

AND

4-10/0

1194 SEA FILE=REGISTRY SUB=L3 SSS FUL L1 L5 STR

L7

G1 C,H

Structure attributes must be viewed using STN Express query preparation. L10 0 SEA FILE=REGISTRY SUB=L5 SSS SAM L7

(FILE 'STNGUIDE' ENTERED AT 17:28:12 ON 22 JAN 2003)

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DEL HIS Y
     FILE 'REGISTRY' ENTERED AT 17:30:12 ON 22 JAN 2003
                STRUCTURE UPLOADED
L1
L2
             50 S L1
          70336 S 1-3/NR AND 0-1/P AND 0/N AND 4-10/O
L3
L4
             50 S L1 SAM SUB=L3
           1194 S L1 FUL SUB=L3
L5
     FILE 'CAPLUS' ENTERED AT 17:33:47 ON 22 JAN 2003
L6
            842 S L5
     FILE 'STNGUIDE' ENTERED AT 17:34:19 ON 22 JAN 2003
     FILE 'REGISTRY' ENTERED AT 17:34:41 ON 22 JAN 2003
     FILE 'STNGUIDE' ENTERED AT 17:35:31 ON 22 JAN 2003
     FILE 'REGISTRY' ENTERED AT 17:36:56 ON 22 JAN 2003
L7
                STRUCTURE UPLOADED
                STRUCTURE UPLOADED
\Gamma8
                STRUCTURE UPLOADED
L9
L10
              0 S L7 SAM SUB=L5
              3 S L7 FUL SUB=L5
L11
             35 S L8 FUL SUB=L5
L12
L13
            610 S L9 FUL SUB=L5
L14
            648 S L11 OR L12 OR L13
        3941227 S 2-5/NC
L15
L16
            648 S L14 SUB=L14
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. . .

FILE 'CAPLUS' ENTERED AT 17:42:23 ON 22 JAN 2003

L17 4 S L11 L18 19 S L12

=> log y
COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION 103.76 387.18 FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL

ENTRY SESSION -14.97 CA SUBSCRIBER PRICE

STN INTERNATIONAL LOGOFF AT 17:43:55 ON 22 JAN 2003

```
ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS
T.18
     2000:706968 CAPLUS
AN
     133:261549
DN
     Cyclic glycerophosphates and analogs for treatment of malignancies
TΙ
     Shinitzky, Meir
IN
     Yeda Research and Development Co. Ltd., Israel
PA
     PCT Int. Appl., 52 pp.
SO
     CODEN: PIXXD2
     Patent
DT
     English
LΑ
FAN.CNT 1
                                           APPLICATION NO.
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                                           _____
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     EP 1162979
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             IE, SI, LT, LV, FI, RO
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                       T2
                            20021126
     JP 2002540145
                            19990325
PRAI IL 1999-129179
                       Α
                            20000324
     WO 2000-IL184
                       W
     MARPAT 133:261549
OS
     Cyclic glycerophosphates as well as some analogs thereof (CGs) are shown
AB
     to increase phosphorylation of intracellular proteins in various cells.
     Such activity is not found with linear .alpha.- or .beta.-
     glycerophosphates. The phosphorylating activity of the CGs render them
     useful in the prevention and treatment of various disorders and diseases
     such as, for example, different kinds of malignancies as well as
disorders
     involving hormone and hormone-like signaling. The CGs are also useful
for
     promotion of target cell differentiation and for detection of abnormal
     conditions in target cells. For example, CHO cells were incubated with 1\,
     or 2 .mu.M of 1,3-cyclic propanediol phosphate for 1, 3, 5, and 10 min at
     37.degree.. The level of tyrosine phosphorylated proteins in the cell
was
     detd. using monoclonal anti-phosphotyrosine antibodies. Phosphorylation
     was most markedly seen in the band(s) having a mol. wt. of .apprx. 35 and
     45 kilodalton.
     298701-05-0P
 IT
     RL: BAC (Biological activity or effector, except adverse); BPN
     (Biosynthetic preparation); BPR (Biological process); BSU (Biological
     study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU
      (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
      (Process); USES (Uses)
         (cyclic glycerophosphates for treatment of malignancies and disorders
         involving hormone-related signaling)
     298701-05-0 CAPLUS
 RN
```

1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide, barium salt (9CI) (CA CNINDEX NAME)

## ●x Ba

IT286020-33-5P

RL: BAC (Biological activity or effector, except adverse); BPR

(Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(cyclic glycerophosphates for treatment of malignancies and disorders involving hormone-related signaling)

286020-33-5 CAPLUS

RN 1,3,2-Dioxaphosphorinan-5-ol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME) CN

L18 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 2000:336094 CAPLUS

DN 133:117815

TI Induction of intracellular signalling by cyclic glycerophosphates and their deoxy analogues

AU Shinitzky, Meir; Haimovitz, Rachel; Nemas, Mara; Cahana, Nava; Mamillapalli, Ramanaiah; Seger, Rony

CS Department of Biological Chemistry, The Weizmann Institute of Science, Rehovot, 76100, Israel

SO European Journal of Biochemistry (2000), 267(9), 2547-2554 CODEN: EJBCAI; ISSN: 0014-2956

PB Blackwell Science Ltd.

DT Journal

LA English

a

AB Cyclic glycerophosphates can be formed by enzymic degrdn. of phospholipids. They have only recently attracted attention, and their physiol. function is still obscure. In this study, we have searched for signalling functions of the natural 1,3-cyclic and 1,2-cyclic glycerophosphates, their deoxy analogs, and the Ph esters of the 1,3-cyclic phosphates. Linear sn-glycerol 3-phosphate and glycerol 2-phosphate served as the control compds. Each of the six-membered ring cyclic phosphates tested induced rapid intracellular tyrosine phosphorylation in CHO and NIH-3T3 cells when applied extracellularly at

concn. of 0.5-4 .mu.M. The phosphorylated intracellular proteins had mol.

masses of .apprxeq. 35 kDa, .apprxeq. 45 kDa, 60-70 kDa and .apprxeq. 120 kDa. The five-membered ring cyclic phosphates had a similar effect, but at an external concn. of 2-10 .mu.M, while sn-glycerol 3-phosphate and glycerol 2-phosphate had no effect. The six-membered cyclic phosphates also induced rapid threonine phosphorylation in CHO cells of .apprxeq. 18-kDa, .apprxeq. 35-kDa, and .apprxeq. 38-kDa proteins. Further expts. indicated that the cyclic phosphates partition rapidly into the cell cytosol where they activate kinases, including mitogen-activated protein kinase. When their intracellular level increases, dephosphorylation presumably takes place. This pattern may account for the signalling profile of cyclic phosphates and suggests that they may take part in processes assocd. with cell differentiation.

TT 42320-97-8 286020-33-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  $\,$ 

study, unclassified); BIOL (Biological study)

(induction of intracellular signaling by cyclic glycerophosphates and their deoxy analogs)

RN 42320-97-8 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 286020-33-5 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 1998:348369 CAPLUS

DN 129:106351

TI Structure of the O-antigen of Vibrio cholerae O155 that shares a putative D-galactose 4,6-cyclophosphate-associated epitope with V. cholerae O139 Bengal

AU Senchenkova, Sof'ya N.; Zatonsky, Georgy V.; Shashkov, Alexander S.; Knirel, Yuriy A.; Jansson, Per-Erik; Weintraub, Andrej; Albert, M. John

CS Karolinska Institute, Clinical Research Center, Huddinge University Hospital, Huddinge, S-141 86, Swed.

SO European Journal of Biochemistry (1998), 254(1), 58-62 CODEN: EJBCAI; ISSN: 0014-2956

PB Springer-Verlag

DT Journal

LA English

AB The O-specific polysaccharide of Vibrio cholerae 0155 was studied by sugar

and methylation analyses, dephosphorylation with 48% hydrofluoric acid, 1H- and 13C-NMR spectroscopy, including two-dimensional COSY, TOCSY, NOESY, and heteronuclear single-quantum coherence (HSQC) expts. The structure of the pentasaccharide repeating unit of the polysaccharide was established. An unusual component, D-galactose 4,6-cyclophosphate, has been reported previously as a component of the capsular polysaccharide

and

O-antigen of V. cholerae O139 Bengal and appears to be responsible for the  $\,$ 

known serol. cross-reactivity between V. cholerae 0139 and 0155.

IT 91740-36-2

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(in structure of O antigen of Vibrio cholerae)

RN 91740-36-2 CAPLUS

CN D-Galactose, cyclic 4,6-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 1996:487442 CAPLUS

DN 125:276356

- TI Studies on the reactivity of bis-glycoaldehyde phosphodiester in alkaline solution
- AU Cook, Stephen D.; Sutherland, John D.
- CS Dyson Perrins Lab., Oxford, OX1 3QY, UK
- SO Tetrahedron Letters (1996), 37(32), 5779-5782 CODEN: TELEAY; ISSN: 0040-4039
- PB Elsevier
- DT Journal
- LA English
- The behavior of bis-glycoaldehyde phosphodiester in alk. soln. has previously been investigated by reducing, dephosphorylating and acetylating the products. The detection of threitol and erythritol tetraacetates by GC coupled with kinetics arguments suggested that bis-glycoaldehyde phosphodiester undergoes rapid intramol. aldolization

give a mixt. of erythrose and threose-2,4-cyclophosphates. In this paper,

electrospray mass spectroscopy, deuteration studies and comparison with synthetic materials are used to confirm and augment these earlier findings.

IT 182256-14-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(studies on intramol. aldolization of bis-glycoaldehyde phosphodiester in alk. soln. by mass spectra)

RN 182256-14-0 CAPLUS

CN D-Xylose, cyclic 3,5-(hydrogen phosphate), monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

IT 182255-92-1P 182255-98-7P 182256-23-1P

RL: SPN (Synthetic preparation); PREP (Preparation) (studies on intramol. aldolization of bis-glycoaldehyde phosphodiester in alk. soln. by mass spectra)

RN 182255-92-1 CAPLUS

CN Methanediol, (2,5-dihydroxy-2-oxido-1,3,2-dioxaphosphorinan-4-y1)-, monosodium salt, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Na

RN 182255-98-7 CAPLUS

CN Methanediol, (2,5-dihydroxy-2-oxido-1,3,2-dioxaphosphorinan-4-yl)-, monosodium salt, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Na

RN 182256-23-1 CAPLUS

CN 1,3,2-Dioxaphosphorinane-4-carboxaldehyde, 2,5-dihydroxy-, 2-oxide, monosodium salt, (4S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Na

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ANSWER 8 OF 19 CAPLUS COPYRIGHT 2003 ACS
     1995:835104 CAPLUS
DN
     124:48797
     Structure of the capsular polysaccharide of Vibrio cholerae 0139 synonym
ΤI
     Bengal containing D-galactose 4,6-cyclophosphate
     Knirel, Yuriy A.; Paredes, Liliana; Jansson, Per-Erik; Weintraub, Andrej;
AU
    Widmalm, Goeran; Albert, M. John
CS
    Karolinska Inst., Huddinge Univ. Hosp., Huddinge, S-141 86, Swed.
    European Journal of Biochemistry (1995), 232(2), 391-6
SO
    CODEN: EJBCAI; ISSN: 0014-2956
PB
    Springer
DT
    Journal
    English
LA
AΒ
    The capsular polysaccharide (CPS) of V. cholerae 0139 synonym Bengal,
    which is thought to carry determinants of O-specificity, was isolated.
    The CPS contained D-galactose, 3,6-dideoxy-L-xylo-hexose (colitose, Col),
     2-acetamido-2-deoxy-D-glucose, 2-acetamido-2,6-dideoxy-D-glucose,
     D-galacturonic acid, and phosphate. The CPS was studied by NMR
     spectroscopy, methylation anal., and selective degrdns., including
partial
     acid hydrolysis at pH 3.1 and dephosphorylation with aq. 48% HF, which
    both resulted in complete cleavage of Col. Thus, CPS is built up of
    hexasaccharide repeating units contq. inter alia D-galactose
     4,6-cyclophosphate and the structure of the V. cholerae CPS proposed by
```

M. Preston et al. (1995) was confirmed.

IT 91740-36-2

L.

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(structure of the capsular polysaccharide of Vibrio cholera 0139 synonym Bengal contg. D-galactose 4,6-cyclophosphate)

RN 91740-36-2 CAPLUS

CN D-Galactose, cyclic 4,6-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ΑN

(18) ANSWER (9) OF 19 CAPLUS COPYRIGHT 2003 ACS 1993:534139 CAPLUS

119:134139 DN

Formation of 1,3-cyclic glycerophosphate by the action of phospholipase C TΙ on phosphatidylglycerol

Shinitzky, Meir; Friedman, Peter; Haimovitz, Rachel ΑU

Dep. Membrane Res. Biophys., Weizmann Inst. Sci, Rehovot, 76100, Israel CS

Journal of Biological Chemistry (1993), 268(19), 14109-15 SO CODEN: JBCHA3; ISSN: 0021-9258

Journal DT

English LΑ

The action of phospholipase C (PLC) from Bacillus cereus on AB phosphatidylglycerol (PG), derived from egg yolk phosphatidylcholine (PC),

was examd. in an ether-water mixt. The PLC cleavage of PG and PC followed

a Michaelis-Menten kinetics with apparent Vmax values per 1 .mu.g enzyme of 0.26 and 0.91 .mu.mol.min-1 and Km values of 10 and 12 mM, resp. When the same enzymic reaction was carried out in minimally buffered aq. soln. of 1% Triton X-100, the decrease in pH with respect to phospholipid cleavage was as expected with PC but much less pronounced with PG. could be accounted for by .alpha.-glycerophosphate, in the PLC hydrolysis of PG. Examn. of the chem. nature of the water-sol. product of PG by 31P NMR revealed a single band at 2.31 ppm, while the bands of .alpha.-glycerophosphate and .beta.-glycerophosphate appeared at 5.12 and 4.57 ppm, resp. Basic hydrolysis of the phospholipase cleavage product

of

PG (0.1 M NaOH for 1 min at 80 .degree.C) followed by neutralization shifted its 31P NMR band to 5.18 ppm, which practically coincided with that of .alpha.-glycerophosphate. Analogous expts. were carried out with PG labeled with 3H at the carbon 2 of the glycerol headgroup ([3H]PG). Autoradiog. of thin layer chromatog. (TLC) of the [3H]PG enzymic hydrolyzate displayed a single 3H-labeled compd., which could be

converted to .alpha.-glycerophosphate by basic hydrolysis. These results strongly suggest that the phosphate headgroup of PG is cleaved off by PLC as 1,3-cyclic glycerophosphate. A series of PLC expts. with phosphatidyldihydroxyacetone and phosphatidyl 1,3-propanediol as model substrates supported this assignment. Two-dimensional homonuclear 1H NMR correlated spectra as well as IR spectra carried out on the isolated sodium salt of this product could further confirm such a structure. The unique structure and chem. nature of 1,3-cyclic glycerophosphate may bear a distinct physiol. function.

TΨ 42320-97-8

RL: FORM (Formation, nonpreparative)

(formation of, by phospholipase C cleavage of phosphatidylglycerol)

42320-97-8 CAPLUS RN

1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME) CN

GΙ

οf

ANSWER 10 OF 19 CAPLUS COPYRIGHT 2003 ACS L181992:59761 CAPLUS ΑN 116:59761 DN Synthesis and testing of sugar phosphofluoridates and cyclic phosphates TI as inhibitors of phosphoglucomutase Percival, M. David; Withers, Stephen G. ΑU Dep. Chem., Univ. British Columbia, Vancouver, BC, V6T 1Y6, Can. CS Journal of Organic Chemistry (1992), 57(3), 811-17 SO CODEN: JOCEAH; ISSN: 0022-3263 DTJournal English LΑ

AB Three aldose phosphofluoridates, e.g. I (R = OH, F), have been synthesized

from the parent phosphate and 2,4-dinitrofluorobenzene, and the mechanism of fluorination has been investigated. Another modified aldose phosphate,

.alpha.-D-glucopyranosyl 4,6-cyclic phosphate [phosphate] has also been synthesized as an analog of 6-phospho-.alpha.-D-glucopyranosyl phosphate. These compds. were tested as possible mechanism-based inactivators of rabbit muscle phosphoglucomutase, but no time-dependent inactivation was obsd. They were, however, found to be reversible inhibitors of phosphoglucomutase, and comparison of their dissocn. consts. with those

the parent phosphates revealed that the removal of a single neg. charge weakens ground-state binding by approx.  $11~\rm kJ/mol$ . Further, the absence of any detectable phosphorylation of these analogs reveals that this second charge is even more important for transition-state interactions, contributing at least 40 kJ/mol to transition-state stability. This suggests that the parent substrates bind to the enzyme and react in their dianionic forms, and it provides a measure of the value of charge-charge interactions at the active site of this key metabolic enzyme.

## IT 138385-97-4

RL: PROC (Process)
(pyridinium salt formation of)

RN 138385-97-4 CAPLUS

CN D-Glucose, cyclic 4,6-(hydrogen phosphate), monoammonium salt (9CI) (CA INDEX NAME)

● инз

RN

(structure of) 105435-62-9 CAPLUS

L18 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS 1986:636193 CAPLUS 105:236193 DN Structure of 5-hydroxy-2-methoxy-1,3,2.lambda.5-dioxaphosphacyclohexane TI 2-oxide ΑU Hamor, T. A. CS Dep. Chem., Univ. Birmingham, Birmingham, B15 2TT, UK Acta Crystallographica, Section C: Crystal Structure Communications (1986), C42(10), 1462-3 CODEN: ACSCEE; ISSN: 0108-2701 DTJournal LΑ English The title compd. is orthorhombic, space group Pna21, with a 10.825(5), b AΒ 9.342(4), and c 6.839(4) .ANG.; dc = 1.61 for Z = 4. The final R = 0.035 for 642 reflections. The 6-membered ring has a distorted chair conformation; the positions of the MeO and OH groups are axial. Angles at P are within 7.5.degree. of tetrahedral. The at. coordinates are given. IT105435-62-9 RL: PRP (Properties)

L18 ANSWER (12 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 1986:591264 CAPLUS

DN 105:191264

TI Structure of two isomeric 1,3,2-dioxaphosphorinanes

AU Jones, A. S.; Kumar, A.; Walker, R. T.

CS Chem. Dep., Birmingham Univ., Birmingham, B15 2TT, UK

SO Journal of Organic Chemistry (1986), 51(22), 4310-11 CODEN: JOCEAH; ISSN: 0022-3263

DT Journal

LA English

OS CASREACT 105:191264

AB The 2 isomer 5-hydroxy-2-methoxy-1,3,2-dioxaphosphacyclohexane 2-oxide were prepd. sep. by stereospecific syntheses, and their structures were confirmed by 13C, 31P and 1H and x-ray crystallog.

IT 104532-42-5P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and configuration of, carbon-13 and phosphorus-31 and proton NMR in relation to)

RN 104532-42-5 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-methoxy-, 2-oxide, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

IT 104532-44-7P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn., crystal structure, and carbon-13, phosphorus-31, and proton NMR of)

RN 104532-44-7 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-methoxy-, 2-oxide, trans- (9CI) (CA INDEX

NAME)

Relative stereochemistry.

L18 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 1982:85915 CAPLUS

DN 96:85915

- TI Analysis of the chirality of oxygen-16, -17, and -18 phosphate esters by phosphorus-31 nuclear magnetic resonance spectroscopy
- AU Jarvest, Richard L.; Lowe, Gordon; Potter, Barry V. L.

CS Dyson Perrins Lab., Oxford Univ., Oxford, OX1 3QY, UK

Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1981), (12), 3186-95 CODEN: JCPRB4; ISSN: 0300-922X

DT Journal

LA English

AB Cyclization of 170- and 180-labeled D-glucose 6-phosphate and adenosine 5'-phosphate to the corresponding conformationally locked 6-membered cyclic phosphate diesters occurs with inversion of configuration, as shown

by comparison of the 31P NMR signals of the cyclic diesters with 170- and 180-labeled phosphate esters of known abs. configuration.

IT 76542-71-7P 76542-72-8P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and NMR of phosphorus in)

RN 76542-71-7 CAPLUS

CN D-Glucose, cyclic 4,6-(methyl phosphate), (S)- (9CI) (CA INDEX NAME)

RN 76542-72-8 CAPLUS

CN D-Glucose, cyclic 4,6-(methyl phosphate), (R)- (9CI) (CA INDEX NAME)

IT 80796-56-1P 80796-59-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and methylation of)

RN 80796-56-1 CAPLUS

CN D-Glucose, cyclic 4,6-(hydrogen phosphate), compd. with pyridine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 2946-06-7 CMF C6 H11 O8 P

CM 2

CRN 110-86-1 CMF C5 H5 N

● K

IT 80796-58-3P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

RN 80796-58-3 CAPLUS

CN D-Glucose, cyclic 4,6-(hydrogen phosphate), compd. with N,N-dioctyl-1-octanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 2946-06-7 CMF C6 H11 O8 P

CM 2

CRN 1116-76-3 CMF C24 H51 N

$$(CH_2) 7^{-}Me$$
  
|  
Me-  $(CH_2) 7^{-}N^{-} (CH_2) 7^{-}Me$ 

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ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS
L18
     1982:20068 CAPLUS
AN
     96:20068
DN
     Synthesis of lipids and their models from glycerol alkylenephosphites.
TI
v.
     Cyclic phosphatidylglycerol and phosphatidyloxyhomocholine
     Predvoditelev, D. A.; Chukbar, T. G.; Zeleneva, T. P.; Nifant'ev, E. E.
ΑU
     Mosk. Gos. Univ., Moscow, USSR
CS
     Zhurnal Organicheskoi Khimii (1981), 17(6), 1305-15
SO
     CODEN: ZORKAE; ISSN: 0514-7492
DT
     Journal
LΑ
     Russian
GΙ
```

Treatment of 1,2-distearoylglycerin with 2-benzylglycerin diethylamidophosphite gave cyclic compd. I (n=0); R= benzyl, which was easily converted to I (n=1, X=0, S). Hydrogenation of I (n=1, X=0, S), R = benzyl) gave I (R=H). Treatment of I (X=0, n=1, R=benzyl) with NMe3 gave the ring cleavage product II (R=benzyl), which was hydrogenated to give II (R=H). II (R=H) was also obtained by reaction of I (n=1, X=0, R=H) with NMe3. Phosphorylation of 1,2-0-isopropylideneglycerin gave phosphite III (n=0), which was oxidized to give III (n=1). 2-Benzylglycerin was also phosphorylated to

give several cyclic compds.

80197-15-5P

TI

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction of, with trimethylamine)

RN 80197-15-5 CAPLUS

CN Octadecanoic acid, 1-[[(5-hydroxy-2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]methyl]-1,2-ethanediyl ester (9CI) (CA INDEX NAME)

L18 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 1981:84399 CAPLUS

DN 94:84399

TI A stereochemical investigation of the cyclization of D-glucose-6[(R)-160,170,180]-phosphate and adenosine-5'[(R)-160,170,180]phosphate

AU Jarvest, Richard L.; Lowe, Gordon; Potter, Barry V. L.

CS Dyson Perrins Lab., Oxford Univ., Oxford, OX1 3QY, UK

Journal of the Chemical Society, Chemical Communications (1980), (23), 1142-5
CODEN: JCCCAT; ISSN: 0022-4936

DT Journal

LA English

AB D-Glucose 6[(R)-160, 170, 180]phosphate (I) and adenosine 5'[(R)-160, 170,

180]phosphate (II) were cyclized [(PhO)2POCl, dioxane, then Bu3N, dioxane]

to give the 4,6-phosphate and 3',5'-phosphate diesters, resp. The reaction occurred with retention of configuration at the P. The abs. configurations of I and II were detd. by 31P-NMR.

IT 76542-71-7P 76542-72-8P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and abs. configuration of, phosphorus NMR in relation to)

RN 76542-71-7 CAPLUS

CN D-Glucose, cyclic 4,6-(methyl phosphate), (S)- (9CI) (CA INDEX NAME)

RN 76542-72-8 CAPLUS

CN D-Glucose, cyclic 4,6-(methyl phosphate), (R)- (9CI) (CA INDEX NAME)

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ANSWER 16/OF 19 CAPLUS COPYRIGHT 2003 ACS
    1980:200147 CAPLUS
AN
    92:200147
DN
ΤI
    Betaine derivatives
    Johnson and Johnson, USA; Mona Industries, Inc.
PΑ
    Neth. Appl., 54 pp.
SO
    CODEN: NAXXAN
DT
    Patent
    Dutch
LA
FAN.CNT 3
                                      APPLICATION NO. DATE
    PATENT NO.
                   KIND DATE
                                      _____
    _____
                        _____
                   ____
                    A 19791107
                                      NL 1979-3526
                                                      19790504
    NL 7903526
PΙ
                   В 19981201
    NL 193247
                        19990402
                    С
    NL 193247
                                      US 1978-902121
                                                      19780505
                   A 19800101
    US 4181634
                   A 19800729
                                      US 1978-965461
                                                      19781130
    US 4215064
                                      US 1978-965462
                                                      19781130
    US 4261911
                    Α
                        19810414
                                      CA 1979-326454
                                                      19790426
                    A1 19811013
    CA 1110640
                                      IN 1979-CA442
                                                      19790501
                    A 19830226
    IN 151133
                                       BE 1979-195007
                                                      19790504
                    A1 19791105
    BE 876055
                                      GB 1979-15709
                                                      19790504
                        19791114
    GB 2020289
                    Α
                    B2 19830112
    GB 2020289
                                                      19790504
                                      BR 1979-2725
    BR 7902725
                    A
                        19791120
                                                      19790504
                    A1 19791130
                                       FR 1979-11364
    FR 2424925
                    B1 19880520
    FR 2424925
                                                      19790504
                                       JP 1979-54116
    JP 55007262
                    A2 19800119
    JP 63040798
                    B4 19880812
                                                      19790504
                                      ES 1979-480266
    ES 480266
                    A1 19800816
                                                      19790504
                    Α
                        19801231
                                       ZA 1979-2156
    ZA 7902156
                                                      19790504
                                       AT 1979-3356
    AT 7903356
                    A.
                        19840515
    AT 376685
                    В
                        19841227
                                                      19790504
                                       CH 1979-4206
                        19850628
    CH 650001
                    Α
                    A1 19791108
                                      AU 1979-46933
                                                      19790511
    AU 7946933
                    B2 19830505
    AU 528547
    US 4380637
                                       US 1982-338728
                                                     19820111
                    Α
                        19830419
                         19780505
PRAI US 1978-902121
    US 1978-965461
                         19781130
                         19781130
    US 1978-965462
                         19780617
    US 1978-807768
                         19791116
    US 1979-95182
GΙ
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HOCH<sub>2</sub>CH<sub>2</sub>N+CH<sub>2</sub>CH(OH)CH<sub>2</sub>OP(O)(ONa)O-C<sub>11</sub>H<sub>23</sub>

AB Surfactants (>35) such as RCONH(CH2)3N+Me2CH2CH(OH)CH2OP(O)(OH)O- (R = C7-17 alkyl) (I), RCONH(CH2)3N+Me2CH2CH2OP(O)(ONa)O- (R = C7-17 alkyl), Me(CH2)10CONH(CH2)3N+Et2CH2CH(OH)CH2OP(O)[OCH2CH(OH)CH2OH]O- [73603-28-8], compd. II [73603-29-9], and Me(CH2)10CONHCH2CH2N+(CH2CH2OH)

ΙI

(CH2CO2Na)CH2CH(OH)CH2OP(O)(ONa)O- [73614-34-3] are prepd. by the reaction of an (alkanamidopropyl)dimethylamine,

2-alkyl-1-(2-hydroxyethyl)-

 $\tilde{2}$ -imidazoline,  $\tilde{N}$ - $(\tilde{2}$ -alkanamidoethyl)- $\tilde{N}$ -(2-hydroxyethyl)glycine, or similar

compd. with ClCH2CH(OH)CH2OP(O)(OH)ONa (III) [1866-22-4], [ClCH2CH(OH)CH2O]2P(O)ONa, ClCH2CH2OP(O)(OH)ONa [73603-14-2], or a similar compd. The surfactants are useful as foaming agents, detergents, antistatic agents, etc. Thus, III and RNH(CH2)3NMe2 (R = coconut acyl) were used to prep. I.

IT 68900-73-2P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation);

RACT

(Reactant or reagent)

(manuf. and reaction of, with tertiary amines)

RN 68900-73-2 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide, monosodium salt (9CI) (CA INDEX NAME)

Na

IT 68900-73-2DP, reaction products with tertiary amines RL: PREP (Preparation)

(manuf. of surface-active)

RN 68900-73-2 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide, monosodium salt (9CI) (CA INDEX NAME)

Na

L18 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 1977:584127 CAPLUS

DN 87:184127

TI Glycero-2-hydroxytrimethylene phosphates

AU Predvoditelev, D. A.; Chukbar, T. G.; Ivanov, V. I.; Nifant'ev, E. E.

CS Mosk. Gos. Pedagog. Inst., Moscow, USSR

SO Zhurnal Organicheskoi Khimii (1977), 13(8), 1612-16 CODEN: ZORKAE; ISSN: 0514-7492

DT Journal

LA Russian

GΙ

AB PhCH2OCH(CH2OH)2 reacted with P(NEt2)3 at 95-120.degree. to give dioxaphosphoranes I (R = NEt2), which reacted with 1,2-isopropylidene-

and

1,3-benzylideneglycerol at 120.degree. to give I (R =

1,2-isopropylidene-3-

and 1,3-benzylidene-2-glyceryloxy). Oxidn. of these with NO gave the corresponding phosphate II, which were hydrolyzed to II (R = 3- and 2-glyceryloxy, resp.), hydrogenolysis of which gave 2'- and 3'-glycero-2-hydroxytrimethylene phosphate.

IT 64528-52-5P 64528-53-6P

RN 64528-52-5 CAPLUS

CN 1,2-Propanediol, 3-[(5-hydroxy-2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]-(9CI) (CA INDEX NAME)

RN 64528-53-6 CAPLUS

CN 1,3-Propanediol, 2-[(5-hydroxy-2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]-(9CI) (CA INDEX NAME)

RN

CN

ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS 1973:431419 CAPLUS ΑN 79:31419 DN Synthesis of sn-glycerol-cyclic-phosphodiester isomers. I TIBuchnea, Dmytro ΑU Banting Best Dep. Med. Res., Univ. Toronto, Toronto, ON, Can. CS Lipids (1973), 8(5), 289-94 SO CODEN: LPDSAP; ISSN: 0024-4201 Journal DTEnglish LA A procedure for the synthesis of stereochem. pure sn-glycerol-cyclic-phosphatediesters was developed. The following isomers were synthesized: AΒ sn-glycerol-2,3-, 1,2-, 1,3-cyclic-phosphate diesters and the racemic mixt. The 2,3- and 1,2-cyclic-phosphate diesters and their racemate are thick liqs. and are unstable; therefore they were converted into Ba(glycerol-cyclic-phosphate diester)2 salts, which can be better stored. The six-membered ring sn-glycerol-1,3-cyclic-phosphate diester is a cryst. stable compd. IT 42320-97-8P RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

1,3,2-Dioxaphosphorinan-5-ol, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

42320-97-8 CAPLUS

- ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS L18
- 1973:418684 CAPLUS AN
- 79:18684 DN
- Preparation and chemistry of 2,6,7-trioxa-1-phosphabicyclo[2.2.1]heptane Denney, Donald B.; Varga, Sandor L. TI
- ΑU
- Sch. Chem., Rutgers State Univ., New Brunswick, NJ, USA CS
- Phosphorus and the Related Group V Elements (1973), 2(5-6), 245-8 SO CODEN: PHUSBV; ISSN: 0369-9722
- Journal DT
- English LΑ
- For diagram(s), see printed CA Issue. GΙ
- HOCH2CH, (OH)CH2OH was heated with (MeO)3P in SF-96 silicone fluid at AΒ 115-120.degree. and the resulting 2,6,7-trioxa-1phosphabicyclo[2.2.1] heptane oxidized with N2O4 to give the trioxaphosphabicycloheptane oxide I. I and MeOH gave the phosphate II.
- 41852-35-1P IT RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)
- 41852-35-1 CAPLUS RN
- 1,3,2-Dioxaphosphorinan-5-ol, 2-methoxy-, 2-oxide (9CI) (CA INDEX NAME) CN

AN

119:134139 DN Formation of 1,3-cyclic glycerophosphate by the action of phospholipase C TIon phosphatidylglycerol Shinitzky, Meir; Friedman, Peter; Haimovitz, Rachel ΑU Dep. Membrane Res. Biophys., Weizmann Inst. Sci, Rehovot, 76100, Israel CS Journal of Biological Chemistry (1993), 268(19), 14109-15 SO CODEN: JBCHA3; ISSN: 0021-9258 Journal DTEnglish LΑ The action of phospholipase C (PLC) from Bacillus cereus on AB phosphatidylglycerol (PG), derived from egg yolk phosphatidylcholine was examd. in an ether-water mixt. The PLC cleavage of PG and PC followed a Michaelis-Menten kinetics with apparent Vmax values per 1 .mu.g enzyme of 0.26 and 0.91 .mu.mol.min-1 and Km values of 10 and 12 mM, resp. When the same enzymic reaction was carried out in minimally buffered aq. soln. of 1% Triton X-100, the decrease in pH with respect to phospholipid cleavage was as expected with PC but much less pronounced with PG. This could be accounted for by .alpha.-glycerophosphate, in the PLC hydrolysis of PG. Examn. of the chem. nature of the water-sol. product of PG by 31P NMR revealed a single band at 2.31 ppm, while the bands of .alpha.-glycerophosphate and .beta.-glycerophosphate appeared at 5.12 and 4.57 ppm, resp. Basic hydrolysis of the phospholipase cleavage product of PG (0.1 M NaOH for 1 min at 80 .degree.C) followed by neutralization shifted its 31P NMR band to 5.18 ppm, which practically coincided with that of .alpha.-glycerophosphate. Analogous expts. were carried out with PG labeled with 3H at the carbon 2 of the glycerol headgroup ([3H]PG). Autoradiog. of thin layer chromatog. (TLC) of the [3H]PG enzymic hydrolyzate displayed a single 3H-labeled compd., which could be converted to .alpha.-glycerophosphate by basic hydrolysis. These results strongly suggest that the phosphate headgroup of PG is cleaved off by PLC as 1,3-cyclic glycerophosphate. A series of PLC expts. with phosphatidyldihydroxyacetone and phosphatidyl 1,3-propanediol as model

ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS

1993:534139 CAPLUS

a distinct physiol. function. IT 149864-37-9

RL: FORM (Formation, nonpreparative) (formation of, by phospholipase C cleavage of phosphatidylhydroxyacetone)

RN 149864-37-9 CAPLUS

CN 1,3,2-Dioxaphosphorinan-5-one, 2-hydroxy-, 2-oxide (9CI) (CA INDEX NAME)

substrates supported this assignment. Two-dimensional homonuclear 1H NMR correlated spectra as well as IR spectra carried out on the isolated sodium salt of this product could further confirm such a structure. The unique structure and chem. nature of 1,3-cyclic glycerophosphate may bear

Y=Q=0)

Ben

(Biological

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ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
L17
     2000:706969 CAPLUS
AN
DN
     133:261536
     Pharmaceutical compositions comprising cyclic glycerophosphates and
TI
     analogs thereof for promoting neural cell differentiation
IN
     Shinitzky, Meir
     Yeda Research and Development Co. Ltd., Israel
PA
     PCT Int. Appl., 42 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 1
                                           APPLICATION NO. DATE
                      KIND DATE
     PATENT NO.
                                            _____
                      ____
                      A2
                            20001005
                                           WO 2000-IL185
                                                            20000324
     WO 2000057865
PΙ
                      A3
                            20010628
     WO 2000057865
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
         W:
             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
             ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                           BR 2000-9296
                                                            20000324
     BR 2000009296
                       Α
                            20011218
                                           EP 2000-912877
                                                            20000324
                       A2
                            20011219
     EP 1162959
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
                            20021126
                                           JP 2000-607616
                                                            20000324
     JP 2002540146
                       T2
PRAI IL 1999-129178
                       Α
                            19990325
                            20000324
     WO 2000-IL185
     MARPAT 133:261536
OS
     Cyclic glycerophosphates and analogs thereof (CGs) are shown to exert
AΒ
     neural promoting activities in target cells. Such activities include
     promotion of neuronal outgrowth, promotion of nerve growth, provision of
     dopaminotrophic supporting environment in a diseased portion of the
brain.
     prevention of nerve degeneration and nerve rescue. These activities of
     the CGs render them useful for treatment of various disorders including
     but not limited to mental disorders such as, for example, schizophrenia,
     dementia or disorders resulting in learning disabilities. In addn.,
these
     CGs may be used for the treatment of neurodegenerative conditions such as
     Alzheimer's disease, Parkinson's disease, conditions resulting from
     exposure to harmful environmental factors or resulting from a mech.
     injury. The CGs may also be used to treat an individual suffering from a
     primary neurodegenerative condition in order to prevent or reduce the
     appearance of secondary degeneration in addnl. nerves ("nerve rescue").
     For example, neural outgrowth of PC12 cells was seen when cells were
grown
     in the presence of nerve growth factor (50 ng/mL) or 1,3-cyclic
     glycerophosphate (1 .mu.M), but not in the presence of linear
     .alpha.-glycerophosphate.
     298701-09-4P 298701-78-7P
     RL: BAC (Biological activity or effector, except adverse); BSU
```

RN

CN

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (compns. comprising cyclic glycerophosphates for promoting neural differentiation for therapeutic uses)
298701-09-4 CAPLUS
1,3,2-Dioxaphosphorinan-5-one, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 298701-78-7 CAPLUS
CN 1,3,2-Dioxaphosphorinan-5-one, 2-hydroxy-, 2-oxide, barium salt (9CI)
(CA INDEX NAME)

●1/2 Ba

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ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
L17
     2002:1329 CAPLUS
AN
     136:325601
DN
     The first synthesis of a cyclic dihydroxyacetone phosphate, a new
TI
molecule
     of biological importance
     Goswami, Shyamaprosad; Adak, Avijit Kumar
ΑU
     Department of Chemistry, Bengal Engineering College (Deemed University),
CS
     Howrah, West Bengal, 711 103, India
     Tetrahedron Letters (2002), 43(3), 503-505
SO
     CODEN: TELEAY; ISSN: 0040-4039
     Elsevier Science Ltd.
PB
DT
     Journal
LΑ
     English
     CASREACT 136:325601
OS
     A six-membered cyclic dihydroxyacetone phosphate (CDHAP)
ΑB
     (2-oxo-2-phenoxy-2.lambda.5-[1,2,3]-dioxaphosphinane-5-one) which is a
new
     and interesting mol. of biol. interest has been synthesized for the first
     time. Though dihydroxyacetone phosphate (DHAP) is very well known and is
     the precursor for enzymic synthesis of sugars, the six-membered cyclic
     dihydroxyacetone phosphate and its synthesis have not been reported to
our
     knowledge. Thus, reaction of (PhO)P(O)Cl2 with CH2:C(CH2OH)2 in CH2Cl2
     gave 5-methylene-2-oxo-2-phenoxy[1,2,3]dioxaphosphorinane which on
     ozonolysis in the presence of DMS in CH2Cl2 gave title compd.,
     2-oxo-2-phenoxy-2.lambda.5-[1,2,3]-dioxaphosphinane-5-one.
IT
     298701-09-4P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of)
RN
     298701-09-4 CAPLUS
     1,3,2-Dioxaphosphorinan-5-one, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)
CN
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RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
L17
AN
     2000:706968 CAPLUS
DN
     133:261549
     Cyclic glycerophosphates and analogs for treatment of malignancies
TI
IN
     Shinitzky, Meir
     Yeda Research and Development Co. Ltd., Israel
PA
SO
     PCT Int. Appl., 52 pp.
     CODEN: PIXXD2
DT
     Patent
LА
     English
FAN.CNT 1
     PATENT NO.
                       KIND DATE
                                             APPLICATION NO. DATE
                                             _____
                      ____
                             _____
                             20001005
                                            WO 2000-IL184
                                                              20000324
                       A2
PΙ
     WO 2000057864
                       A3
                             20010531
     WO 2000057864
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                        A2 20011219
                                           EP 2000-912876
                                                               20000324
     EP 1162979
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
                                             JP 2000-607615
                                                               20000324
                             20021126
     JP 2002540145
                      T2
                             19990325
PRAI IL 1999-129179
                        Α
                             20000324
     WO 2000-IL184
                        W
     MARPAT 133:261549
OS
     Cyclic glycerophosphates as well as some analogs thereof (CGs) are shown
AΒ
     to increase phosphorylation of intracellular proteins in various cells.
     Such activity is not found with linear .alpha. - or .beta. -
     glycerophosphates. The phosphorylating activity of the CGs render them
     useful in the prevention and treatment of various disorders and diseases
     such as, for example, different kinds of malignancies as well as
disorders
     involving hormone and hormone-like signaling. The CGs are also useful
for
     promotion of target cell differentiation and for detection of abnormal
     conditions in target cells. For example, CHO cells were incubated with 1
     or 2 .mu.M of 1,3-cyclic propanediol phosphate for 1, 3, 5, and 10 min at
     37.degree.. The level of tyrosine phosphorylated proteins in the cell
was
     detd. using monoclonal anti-phosphotyrosine antibodies. Phosphorylation
     was most markedly seen in the band(s) having a mol. wt. of .apprx. 35 and
     45 kilodalton.
     298701-09-4P 298701-78-7P
     RL: BAC (Biological activity or effector, except adverse); BPR
(Biological
     process); BSU (Biological study, unclassified); PRP (Properties); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
     PREP (Preparation); PROC (Process); USES (Uses)
         (cyclic glycerophosphates for treatment of malignancies and disorders
         involving hormone-related signaling)
     298701-09-4 CAPLUS
RN
```

CN 1,3,2-Dioxaphosphorinan-5-one, 2-phenoxy-, 2-oxide (9CI) (CA INDEX NAME)

RN 298701-78-7 CAPLUS
CN 1,3,2-Dioxaphosphorinan-5-one, 2-hydroxy-, 2-oxide, barium salt (9CI)
(CA INDEX NAME)

●1/2 Ba